COMPARATIVE STUDY OF FASTING PLASMA INSULIN LEVEL BETWEEN NORMOTENSIVES AND PREECLAMPTIC WOMEN

Dissertation submitted to

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In partial fulfillment of the regulations
For the award of the degree of

M.S. BRANCH-II
OBSTETRICS AND GYNAECOLOGY

MADRAS MEDICAL COLLEGE

APRIL 2016

BONAFIDE CERTIFICATE

This is to certify that the dissertation entitled **"COMPARATIVE STUDY OF FASTING PLASMA INSULIN LEVEL BETWEEN NORMOTENSIVES AND PREECLAMPTIC WOMEN"** is a bonafide record work done by **Dr. P.S.KOTTEESWARI** under my direct supervision and guidance, submitted to The Tamil Nadu Dr. MGR Medical university in partial fulfillment of university regulations for M.S Obstetrics and Gynaecology.

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DECLARATION

I, **Dr. P.S.KOTTEESWARI,** solemnly declare that the dissertation titled **"COMPARATIVE STUDY OF FASTING PLASMA INSULIN LEVEL BETWEEN NORMOTENSIVES AND PREECLAMPTIC WOMEN"** has been prepared by me. I also declare that this bonafide work or a part of this work was not submitted by me for any award, degree,diploma to any other university either in India or abroad.

This is submitted to The Tamil Nadu Dr. MGR Medical University, Chennai in partial fulfillment of the rules and regulations for the award of M.S Degree (Obstetrics and Gynaecology) held in APRIL 2016.

Place :

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CONTENTS

Introduction

INTRODUCTION

Preeclampsia is pregnancy specific syndrome that can affect virtually every organ system, characterized by hypertension and proteinuria in pregnant women with no prior incidence of these sequences which remits after delivery. Appearance of proteinuria remains an important objective diagnostic criterion.

Criteria for diagnosis of preeclampsia:

1) Systolic blood pressure of 140mmHg or higher and diastolic blood pressure of 90mmHg or higher that occurs after 20wks of gestation in a women with previously normal BP.
2) Proteinuria defined as urinary excretion of 0.3g protein or higher in a 24hrs urine specimen.

PE associated with abnormal or deficient placentation leading to increased vascular resistance and reduced placental perfusion. These changes are due to endothelial dysfunction. However the factor that cause the disturbance has not been identified.

In normal pregnancy, there will be increased fasting plasma insulin level, especially maximum in third trimester. Probably due to increased amount of several insulin antagonistic hormones such as Human placental lactogen,[1,2] progesterone[3] and Carticotrophin releasing hormones[4].

Insulin is a polypeptide hormone secreted by β-cells of pancreas. Insulin formed after elimination of C peptide by hydrolysis. It is made up of 2 chains of 21 & 30 AA connected by 2 disulfide bridges.

The pregnancies complicated by hypertension; there is an exaggeration of Insulin resistance and associated metabolic changes.

Cardiovascular research showed that there is increased evidence suggestive of hyperinsulinemia can causes increased endothelial damage resulting in atherosclerotic changes in the vessels.

The aim of the study to test hypothesis that fasting plasma insulin levels are increased in women with preeclampsia as compared to normotensive women.

Aim & objectives of the study

OBJECTIVES OF THE STUDY

1. To compare the levels of Fasting plasma insulin levels in preeclampsia women and normotensive pregnant women.
2. To assess the elevation of fasting plasma insulin levels in relation to the severity of preeclampsia.

Review of Literature

REVIEW OF LITERATURE

Preeclampsia is syndrome of endothelial dysfunction, that can affect any organ system. The disease may also be associated with a variety of other signs and symptoms such as leg edema, visual disturbances, vomiting, headache ,right hypochondriac and epigastric pain.

Preeclampsia characterized by hypertension, proteinuria[7] and activation of the hemostatic system which regress after delivery. It is one of the most major cause of maternal, perinatal morbidity and mortality.

This is a disorder of multiorgan system that can affect virtually every organ and system in the body. It is representation of complex disease process involving nearly the entire system of our body.

This is most commonly seen in primigravidas and resolves within several days after delivery. The exact etiology of the disease is not known, although a numerous studies have been put forward.

Endothelial cell injury[5,6] and altered endothelial cell function appears to play an important role in the pathogenesis of all aspects of the multisystem damage[8] as seen in preeclampsia. Preeclamptic women having hyperinsulin that is reflected by higher plasma insulin level compared to normal pregnant women. It was hypothesized that hyperinsulinemia contributes to the pathogenesis of the disease by exerting its effects on glomerular filtration rate, Renal blood flow , Plasma aldosterone concentration and urinary sodium exertion. Fasting plasma insulin levels were higher in the women during their early third trimester which was commonly associated with increased risk of preeclampsia. The study results suggested that insulin resistance and associated hyperinsulinemia plays a pivotal role in the pathogenesis of hypertension complicating pregnancy.

Classification of Hypertension in pregnancy:

The incidence of hypertensive disorders in pregnancy varies between 5-10% and it is in raising trend since women are postponing their first pregnancy to a later age and increased pre-pregnancy weight. High blood pressure is a sign not a disease and it reflects an increase in cardiac output or more commonly increased peripheral resistance.

Various schemes of classifying hypertensive disorders in pregnancy have been proposed by different obstetric and hypertension societies.

The National Institute of Health (NIH) working group of the NHBPEP – National High Blood Pressure education programme (2000)[8] categorized hypertensive disorders into five types.

I. Gestational Hypertension:

- BP $\geq$ 140/90mmHg for the first time in pregnancy after 20 weeks of gestation.
- BP returns to normal within 3 months after delivery.
- There is no proteinuria
- Patient might have other signs of preeclampsia like headache or thrombocytopenia.

II. Preeclampsia (New Hypertension and Quantified Proteinuria)

1. **Basic (Least Criteria)**
    - BP -140/90 mmHg or more after 20 weeks gestation
    - Proteinuria $\geq$ 300mg/24hrs or persistent 1+ or more on dipstick random sample

2. Definitive Criteria

- BP > 160/110mmHg
- Proteinuria 2+ on dipstick or 2 gm in 24 hrs urine
- Raised Serum Creatinine (>1.2mg/dl)
- Platelets <100000/mm3
- Microangiopathic hemolysis – increased LDH
- Elevated liver enzymes – AST and ALT
- Persistant headache or other cerebral or visual disturbance
- Persistantepigastric pain

III. Eclampsia

Development of convulsion in case of preeclampsia in the absence of other causes of convulsions.

IV. Superimposed preeclampsia on chronic hypertension

- New onset proteinuria ≥ 300 mg/24hrs in hypertensive women but no proteinuria before 20 weeks gestation.
- A sudden increase in blood pressure or proteinuria or thrombocytopenia (Platelet count <100000/mm3) in women with hypertension and proteinuria before 20 weeks of gestation.

V. Chronic Hypertension

- Bp≥140/90 mmHg before pregnancy or diagnosed before 20 weeks gestation in absence of gestational trophoblastic disease.
- Hypertension first diagnosed after 20 weeks but persisting after 12 weeks post partum.

Incidence[8,9]

Gestational hypertension – 5%

Preeclampsia – 5-10% of all pregnancies

Eclampsia – 0.5-2%

Superimposed preeclampsia on chronic hypertension – 25%

Hypertension – 1-2%

Characteristics	Mild preeclampsia	Severe Preeclampsia
Symptoms		
1. Epigastric or upper abdominal pain	Nil	Present
2. Headache	Nil	Present
3. Convulsion	Nil	May be present
4. Visual or cerebral disturbances	Nil	Present

Signs		
1. Systolic BP	<160mmHg	≥160mmHg
2. Diastolic BP	<110mmHg	≥110mmHg
3. Oliguria	Absent	Present
4. Fetal growth restriction	Absent	Present
5. Brisk tendon reflexes or clonus	Absent	Present
6. Cardiac dysfunction with pulmonary edema	Absent	Present
Investigations		
1. Proteinuria	Trace to 1+	2+ or more
2. Platelet Count	Normal	Decreased (<100000/mm^3)
3. Evidence of hemolysis	Absent	Present
4. Elevated serum transaminase levels (AST, ALT)	Absent	Present
5. Serum creatinine	Normal	Raised

RISK FACTORS FOR PRE-ECLAMPSIA[10]

1) Age and Parity:
    a. Nulliparity
    b. Long inter pregnancy interval
    c. Extremes of age (Teenage pregnancy / Pregnancy >40yrs)

2) Genetic predisposition
    a. Family history of preeclampsia
    b. Race and ethinicity – preeclampsia more common in blacks and Asians.

3) Secondary to underlying disorders
    a. Diabetes Mellitus
    b. Renal disease
    c. Chronic hypertension
    d. Obesity (BMI >35kg/m^2)
    e. Collagen vascular disorders
    f. Hyperhomocysteinemia
    g. Antiphospholipid antibodies
    h. Factor V Leiden deficiency
    i. Protein C and S deficiency

4) Pregnancy related risk factors

    a. Molar pregnancy
    b. Hydropsfetalis
    c. Multiple pregnancy
    d. UTI

5) Partner – related factors

    a. Donor insemination
    b. Limited exposure to sperm
    c. Partner changing

ETIOLOGY

Preeclampsia is a multifactorial disorder. The exact etiology remains unknown. Numerous non mutually exclusive hypothesis have been explored some of the accepted hypothesis of etiopathogenesis include:

i) Abnormal trophoblastic invasion and placental ischemia theory

ii) Immunological theory[11]

iii) Genetic imprinting[12]

iv) Nutritional factors[13-16]

v) Vascular and inflammatory changes due to maternal maladoptation[17,22,23,24]

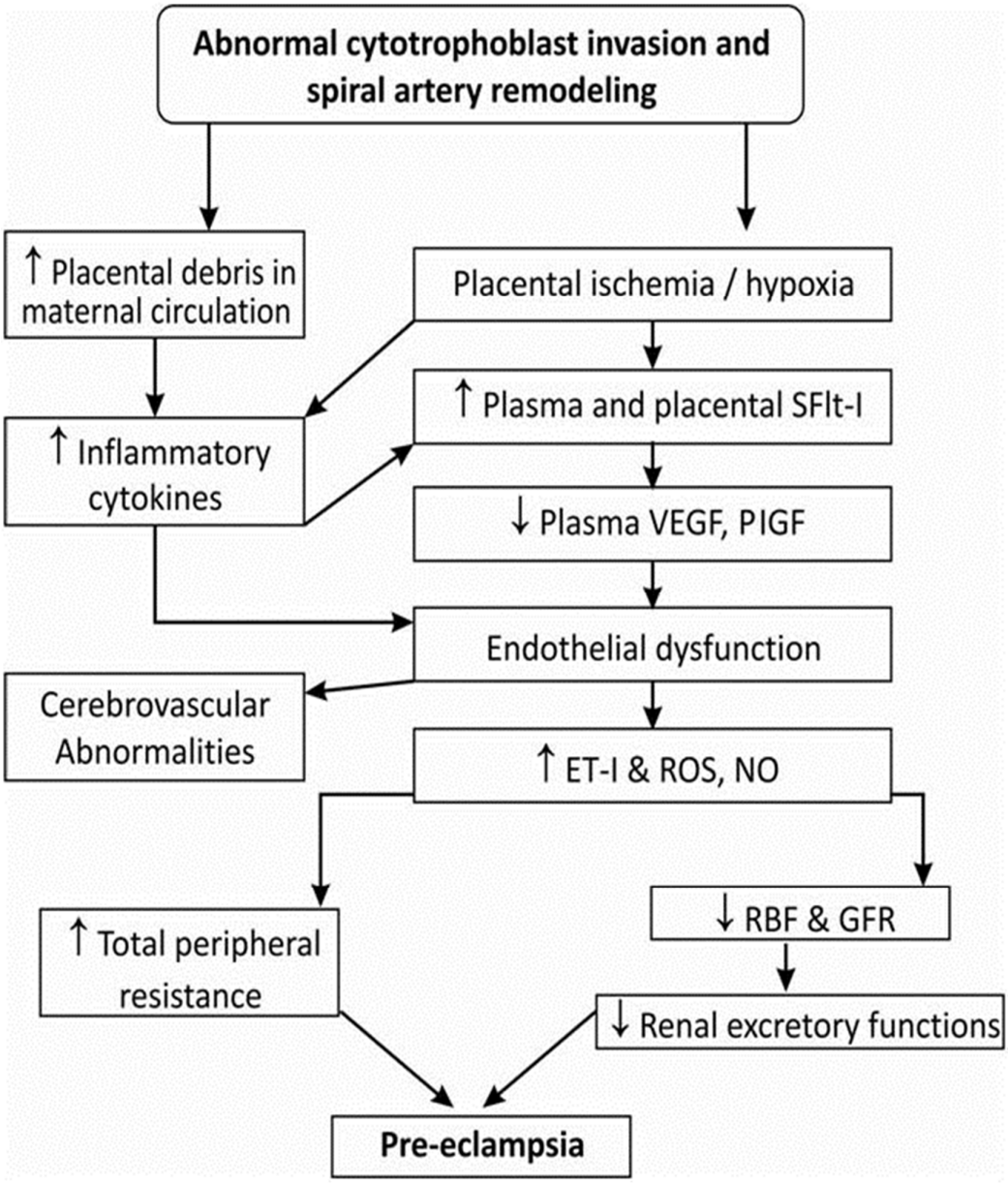
vi) Intervention of various factors

vii) Endothelial cell activation[17-21]

Preeclampsia during pregnancy occurs more often;

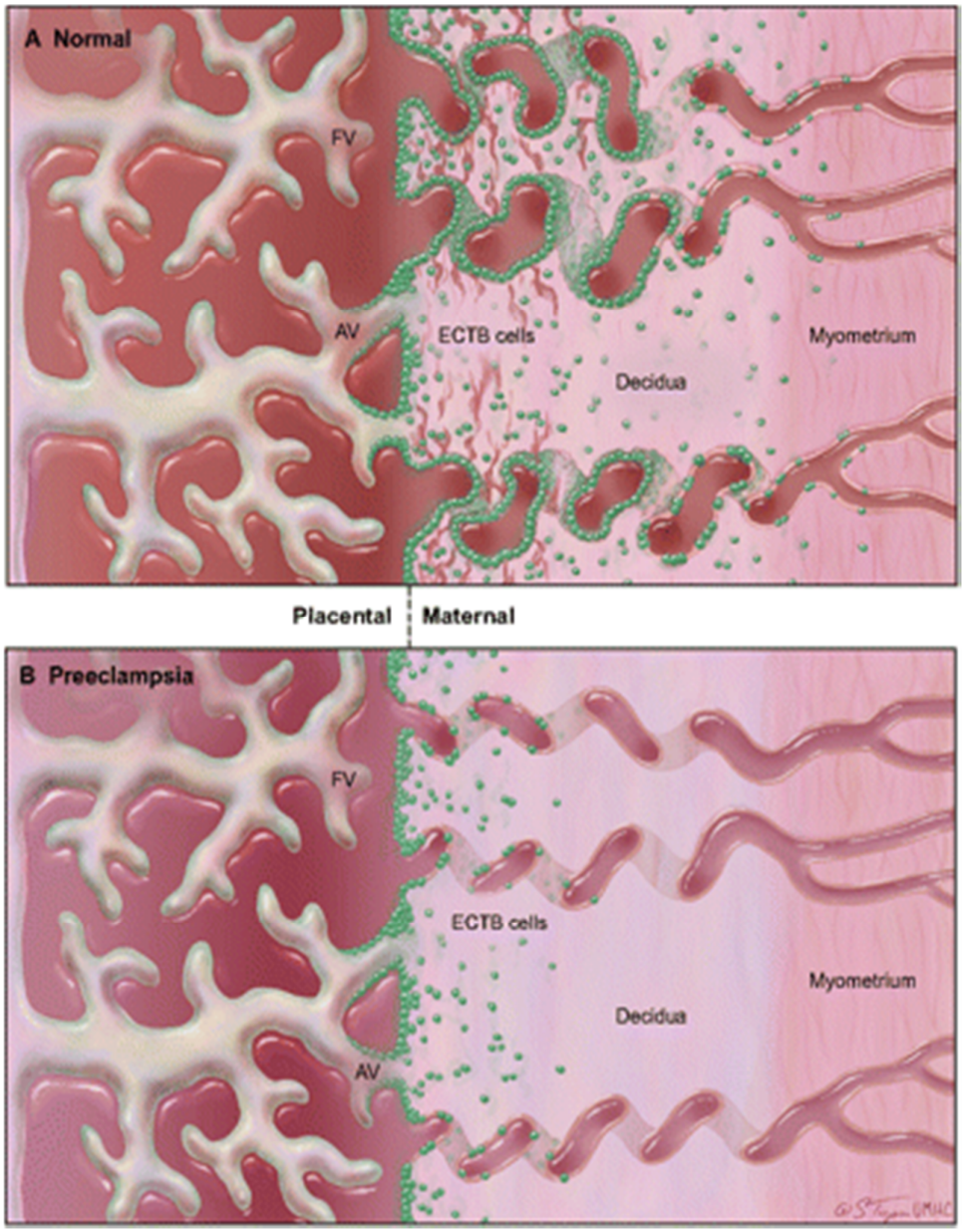
a) In women exposed to the chorionic villi for the first time;
b) In women exposed to excess of chorionic villi. (e.g. Multiple pregnancy and hydatidifrom mole).
c) Have preexisting renal or cardiovascular disease
d) Genetically predisposed women

Several recent studies showed that insulin resistance many also play a role in pathogenesis of preeclampsia and suggest parallels between preeclampsia and insulin resistance.

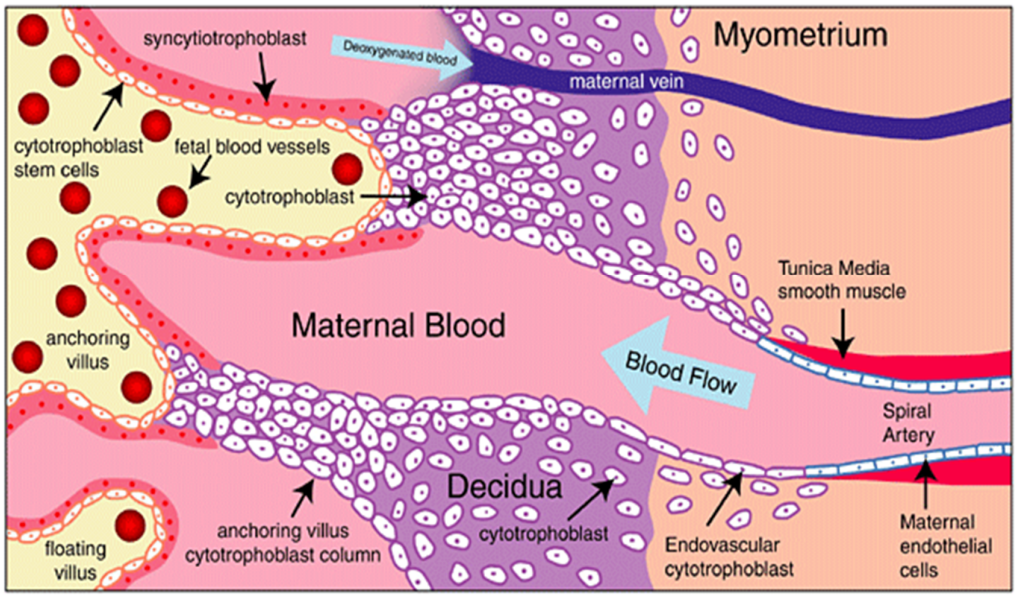


(ET -1- Endothelin -1, PIGF- Placental Growth factor, ROS- Reactive Oxygen species, SFLT- 1- Soluble Fms like Tyrosine Kinase-1, VEGF- Vascular Endothelial Growth Factor)

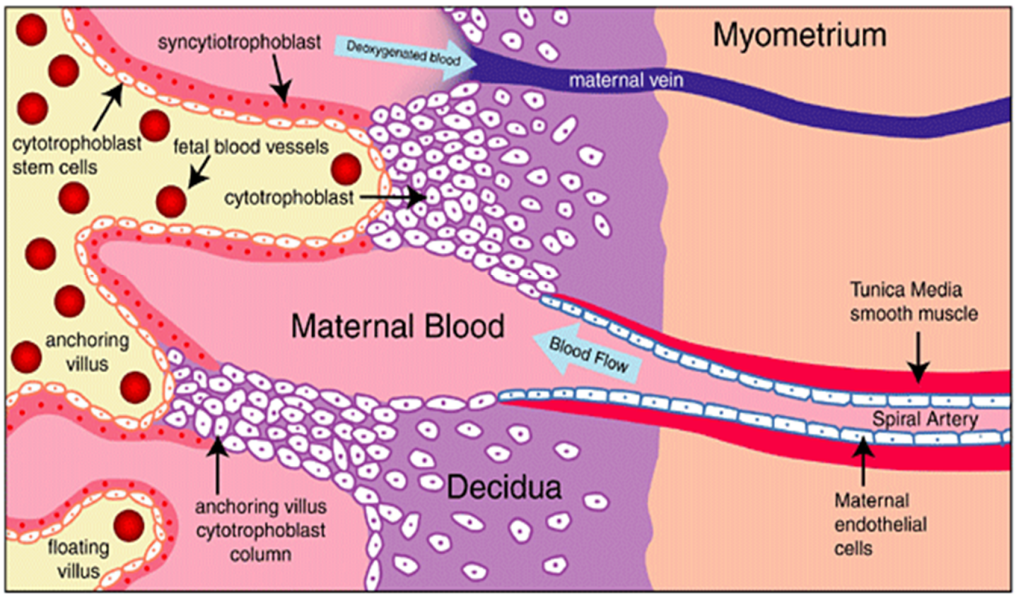
1. Abnormal trophoblastic invasion and placental ischemia theory



Normal



Preeclampsia



The uterine spiral arterioles undergo extensive changes during pregnancy as they are invaded by endovascular trophoblasts. These cells replace the vascular endothelial lining to increases diameter of vessel in case of normal implantation. In preeclampsia; however there may be incomplete trophoblastic invasion of decidual vessels, but not myometrial vessels and their mean diameter is only half that of vessels in normal placentas. Abnormally narrow spiral arteriolar lumen impairs placental blood flow. The decreased placental perfusion and hypoxic environment leads to placental debris. That incites a systemic inflammatory response in patients with preeclampsia.

2) Immunological theory:[11]

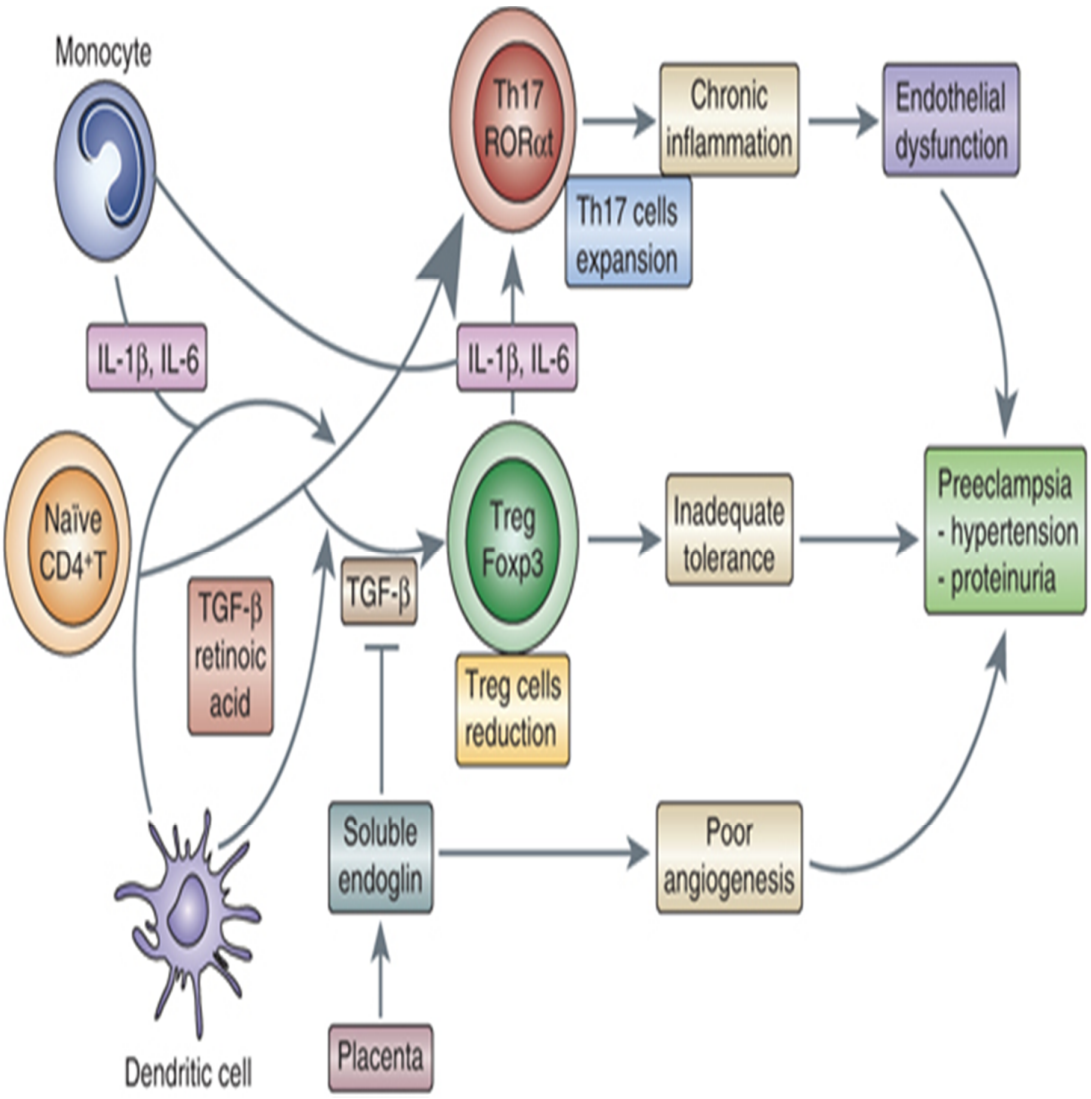
Normal placentation required a balance between maternal immune response and fetal allograft. Hence these balance might be disturbed in case of preeclampsia thus the endovascular trophoblastic invasion of spiral arteries in the myometrial segment does not occur resulting in fetoplacentalhypoperfusion in later stages of pregnancy.

Past exposure to paternal antigen (fetal cells and placenta) is protective against preeclampsia which explains higher incidence of preeclampsia in primigravidas and in pregnancies on change of partner or on donated sperm.

Some examples of inherited immunogenetic factors that many modify phenotype and genotype expression in preeclampsia.

a) Immunization from prior gestation
b) Inherited haplotypes for NK cells receptors – also called killer – immunoglobulin like receptor.
c) Inherited haplotypes for HLA-A, B, D, Ia, II
d) Possibly shared susceptibility genes with chronic hypertension and diabetes.

A study recently reviewed the possible role of immune maladaptation in pathophysiology of preeclampsia. Right from early second trimester, women who expected to develop preeclampsia have a significantly lower proportion of helper ‘T’ cells (Th1) compared with that of women who remains normotensive.

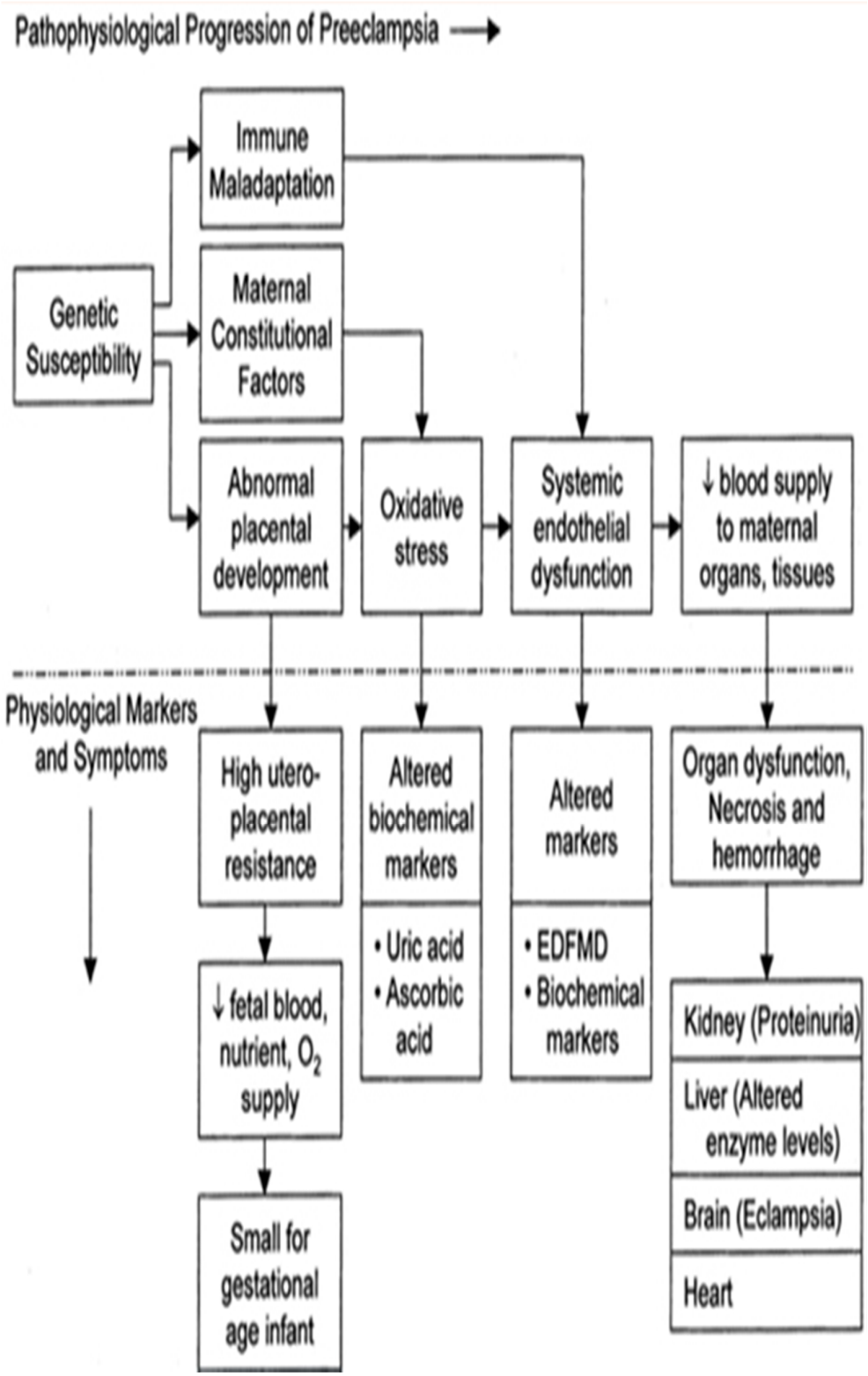


3) Genetic Imprinting:[12]

Preeclampsia is a polygenic and multifactorial disorder. The predisposition to hereditary hypertension might be linked to preeclampsia and the tendency for preeclampsia-eclampsia has been initiated.

Genetic predisposition can be involved in

- Single recessive gene with a frequency of 0.25
- Genes involved in placental vascular injury / blood pressure regulation / placental vascular remodeling such as.
    - TNF-αgene (Tumour necrosis factor – alpha gene)
    - ET-1gene (Endothelin-1 gene)
    - Ag 1 gene(Angiotensinogen gene - T235)
    - E-Nos gene (Endothelial Nitric oxide synthetase gene)


Pathophysiological Progression of Preeclampsia
Immune Maladaptation
Genetic Susceptibility
Maternal Constitutional Factors
Abnormal placental development
Oxidative stress
Systemic endothelial dysfunction
↓ blood supply to maternal organs, tissues
Physiological Markers and Symptoms
High utero-placental resistance
Altered biochemical markers
Altered markers
Organ dysfunction, Necrosis and hemorrhage
• Uric acid
• Ascorbic acid
• EDFMD
• Biochemical markers
↓ fetal blood, nutrient, O_2 supply
Kidney (Proteinuria)
Liver (Altered enzyme levels)
Brain (Eclampsia)
Heart
Small for gestational age infant

4) Nutritional Factors:[13-16]

Dietary excess or deficiency have been blamed as the cause of preeclampsia. However dietary taboos that have been implicated in association with preeclampsia are diary products, meat, protein, purines, fat, salts and other elements.

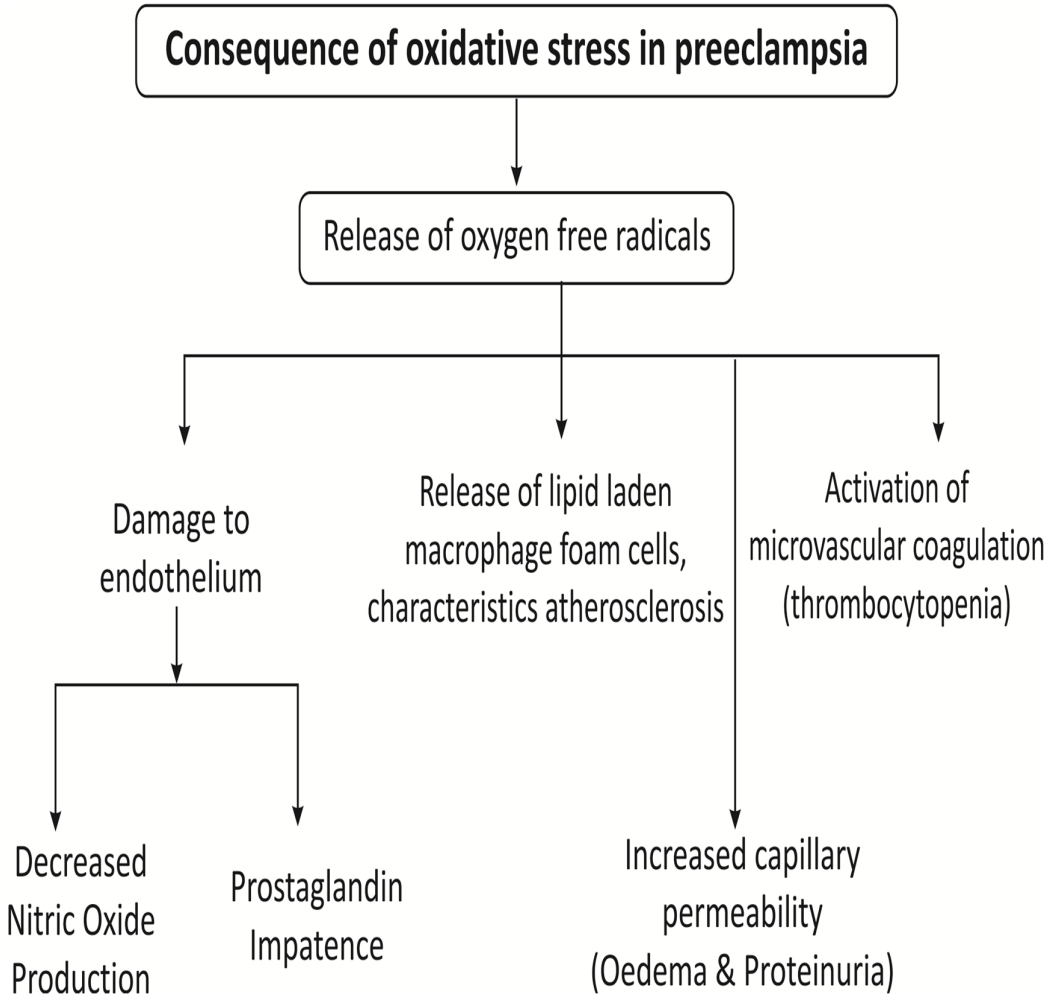
5) Vascular and inflammatory changes due to maternal maladaptation[17,22,23,24]

Placental ischemic changes associated with increased level of cytokines and interleukin levels which play as a oxidative stress[22] marker associated with preeclampsia. The following oxidative stress markers[25,26] found to be increased in preeclampsia such as

a) Malonyldialdehydes
b) Glutathione peroxides
c) Superoxide dismutase

Antioxidants have been found to be reduced in

a) Lycopene
b) Vitamin C



6) Endothelial cell Activation: [17-21]

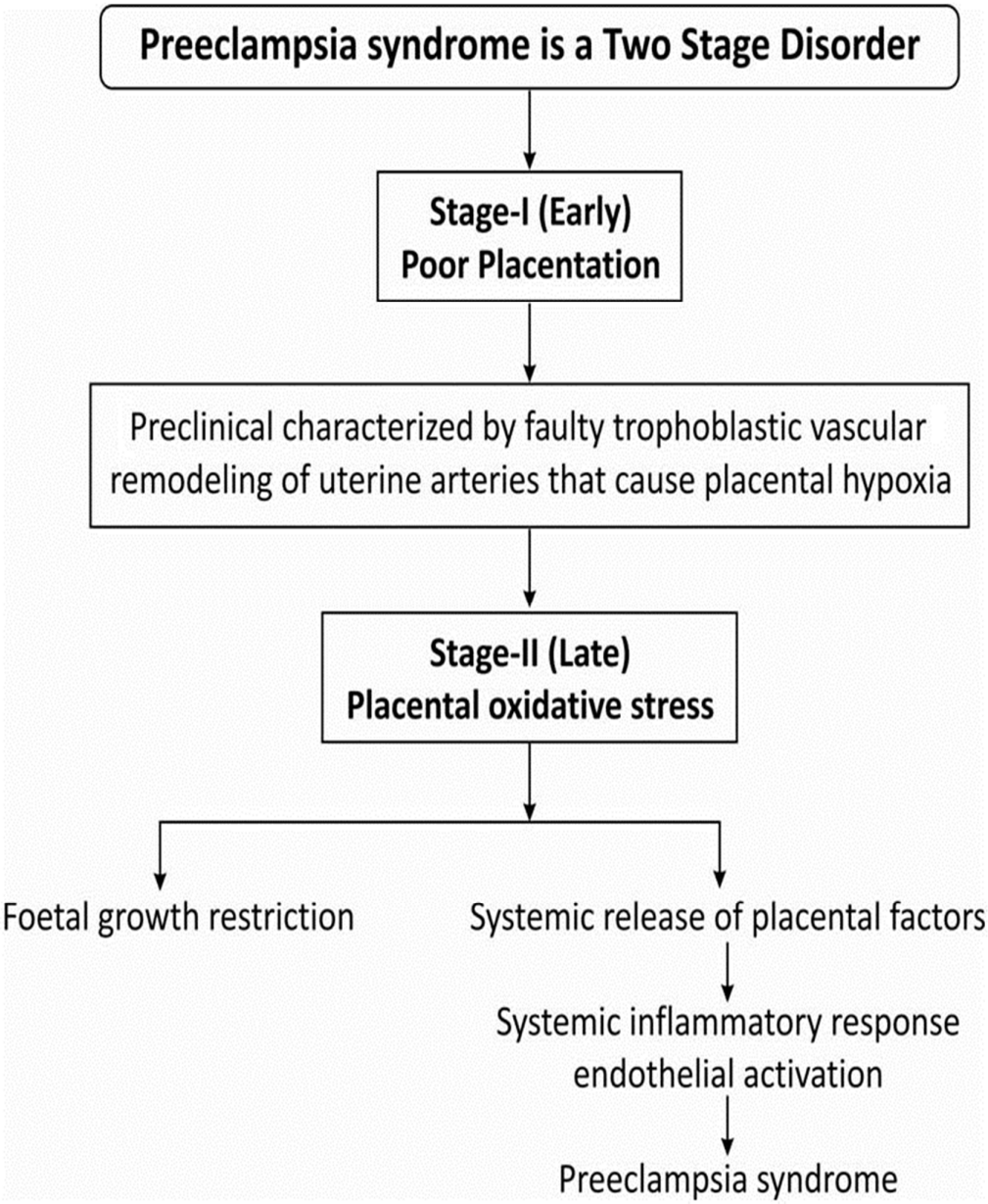
It has been proposed that endothelial cell dysfunction[17] is due to an extreme activated state of leukocytes in the maternal circulation.

Normal maternal vascular endothelium lined by single squamous epithelium which covers the luminal side of blood vessels respond to relaxing and contracting factors which maintains vascular hemostasis.

Cardiovascular research showed with increased evidence that hyperinsulinemia can cause endothelial dysfunction which leads to increase in the formation of endothelial and thromboxane which increases sensitivity of vascular endothelium to angiotensin II and decreased the level of prostacyclin (Vasodilator).

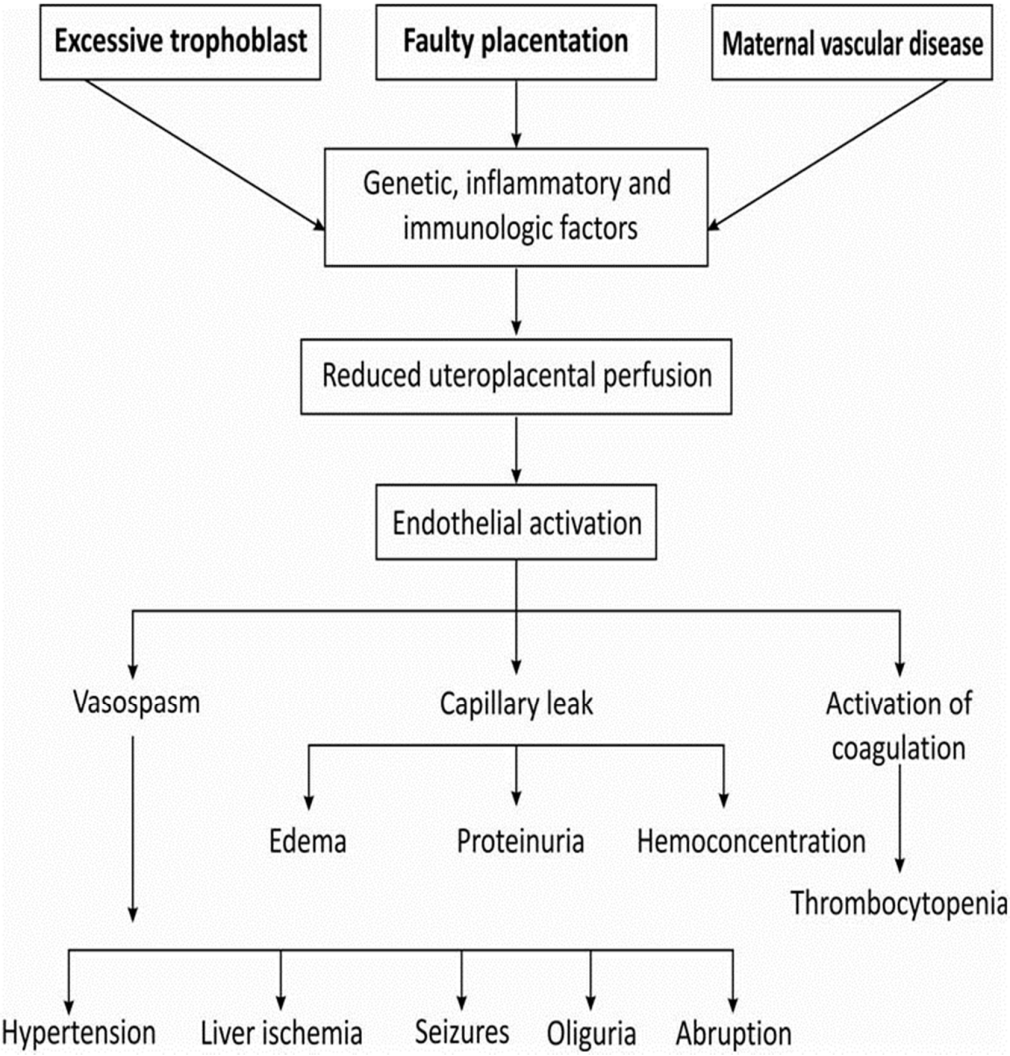
- It has been hypothesized that hyperinsulinemia contributes to the pathogenesis of the disease by its effects on urinary Na+ excretion, Glomerular filtration rate, Renal blood flow and plasma aldosterone concentration.

- There is a functional imbalance[18] between vasodilator and vasoconstrictor in preeclampsia.


Preeclampsia syndrome is a Two Stage Disorder
Stage-I (Early)
Poor Placentation
Preclinical characterized by faulty trophoblastic vascular remodeling of uterine arteries that cause placental hypoxia
Stage-II (Late)
Placental oxidative stress
Foetal growth restriction
Systemic release of placental factors
Systemic inflammatory response endothelial activation
Preeclampsia syndrome

PATHOPHYSIOLOGY OF PREECLAMPSIA

It is a dynamic and progressive process. It is a syndrome with multiorgan system involved with adverse fetal and maternal effects. All mechanism are interrelated provide positive feed back leading to further vascular damage. Thus establishing a visious cycle.



PATHOGENESIS

1) VASOSPASM:

Vasospasm plays a crucial role in pathogenesis of preeclampsia – eclampsia and is based upon the direct observation of small blood vessels in the nail beds, ocular fundi and bulbar conjunctiva. It also shows histological changes in various organ system. Generalised vascular constriction leads to increased vascular resistance to blood flow which lead on to hypertension.

Vasospasm

↓

Increased resistance to blood flow

↓

Endothelial damage

↓

Inter endothelial leaks through which blood constituents, platelets and fibrinogen are deposited sub endothelially

↓

Ultra structural changes in the sub endothelial region of resistance vessels

↓

Diminished blood flow

↓

Ischemia of surrounding tissues

↓

End organ disturbance

2.INCREASED PRESSOR RESPONSE:[18]

Normal pregnant women develops refractoriness to vasopressor agents. The refractoriness in normal pregnancy is due to the downregulation of the angiotensin receptors present in the vascular smooth muscle. There is evidence support that abalance between the production and metabolism of the vasoactive prostoglandin is responsible for maintenance of vascular refractoriness.

Moreover increased sensitivity to angiotensin II clearly proceeds the onset of gestational hypertension. Women with preeclampsia lost this refractoriness several weeks before the onset of hypertension.

3.NITRIC OXIDE:

The effects of nitric oxide production in preeclampsia is unclear. It is a potent vasodilator synthesized from L.Arginine by endothelial cells. In normal pregnant women, nitric oxide maintains the normal low pressure vasodilated state characteristic of fetoplacental perfusion.

Preeclampsia

↓

Decreased endothelial nitric oxide synthase expression

↓

Increasing nitric oxide inactivation

↓

Increases mean arterial pressure, decrease HR

↓

Reverses the pregnany – induced refractoriness to vasopressors

4.ENDOTHELINS:

Endothelins are 21 amino acid peptides are potent vasoconstrictors. Endothelin-I [24] produced by human endothelium and have found to be increased in preeclampsia.

5.PROSTOGLANDINS:

When compared with normal pregnancy; endothelial prostacyclin (PGI_2) production is decreased, Thromboxane A2 secretion increased. In preeclampsia prostacyclin: Thromboxane A2 ratio decreases. The net results favors increased sensitivity to angiotensin II resulting in vasoconstriction.[23]

PATHOPHYSIOLOGICAL CHANGES

1) UTEROPLACENTAL INSUFFICIENTLY:

a) Vasospasm of utero placental vasculature causes intrauterine growth restriction, placental infarction, iatrogenic prematurity and abruptio placentae.

b) There is premature ageing of placenta and areas of infarcts seen on the maternal surface of placenta on histopathological examination.

2) CARDIOVASCULAR CHANGES

Due to generalized vasospasm, the normal hypervolemia of pregnancy is not seen in preeclampsia as a result of which there is decreased cardiac preload. Cardiac output is decreased because of decreased in preload and increased after load. Central venous pressure and pulmonary capillary wedge pressure is reduced in preeclamptic women.

3) VOLUME HOMEOSTASIS[17] : FLUID AND ELECTROLYTE CHANGES[17]

Edema in preeclampsia is due to expanded extracellular fluid which is possibly due to endothelial injury. Reduced plasma oncotic pressure play a important role in these women causes infiltrationimbalance causing further displacement of intravascular fluid

into the extravascular space. There is no electrolyte imbalance unless there is fluid overload or excessive administration of diuretics.

4) ENDOCRINE CHANGES:[17]

Plasma levels of renin, angiotensin II and aldosterone are reduced to non pregnant levels in women with preeclampsia. But their blood vessels are more sensitive to their chemical substances. Inspite of decrease in aldosterone level, there is increase in the sodium retention.

5) RESPIRATORY CHANGES:

a) Pulmonary edema

b) ARDS (Adult respiratory distress syndrome)

c) Chemical pneumonitis

d) Scattered alveolar hemorrhages

e) Pneumonia

6) HAEMATOLOGICAL CHANGES:[17]

Haematological abnormalities develop in some women with preeclampsia in the form of

i) Thrombocytopenia (most common)[17]

ii) Microangiopathic hemolytic anemia

iii) Increased blood viscoscity

iv) Hemoconcentration

v) Disseminated intravascular coagulation

PROTEINURIA

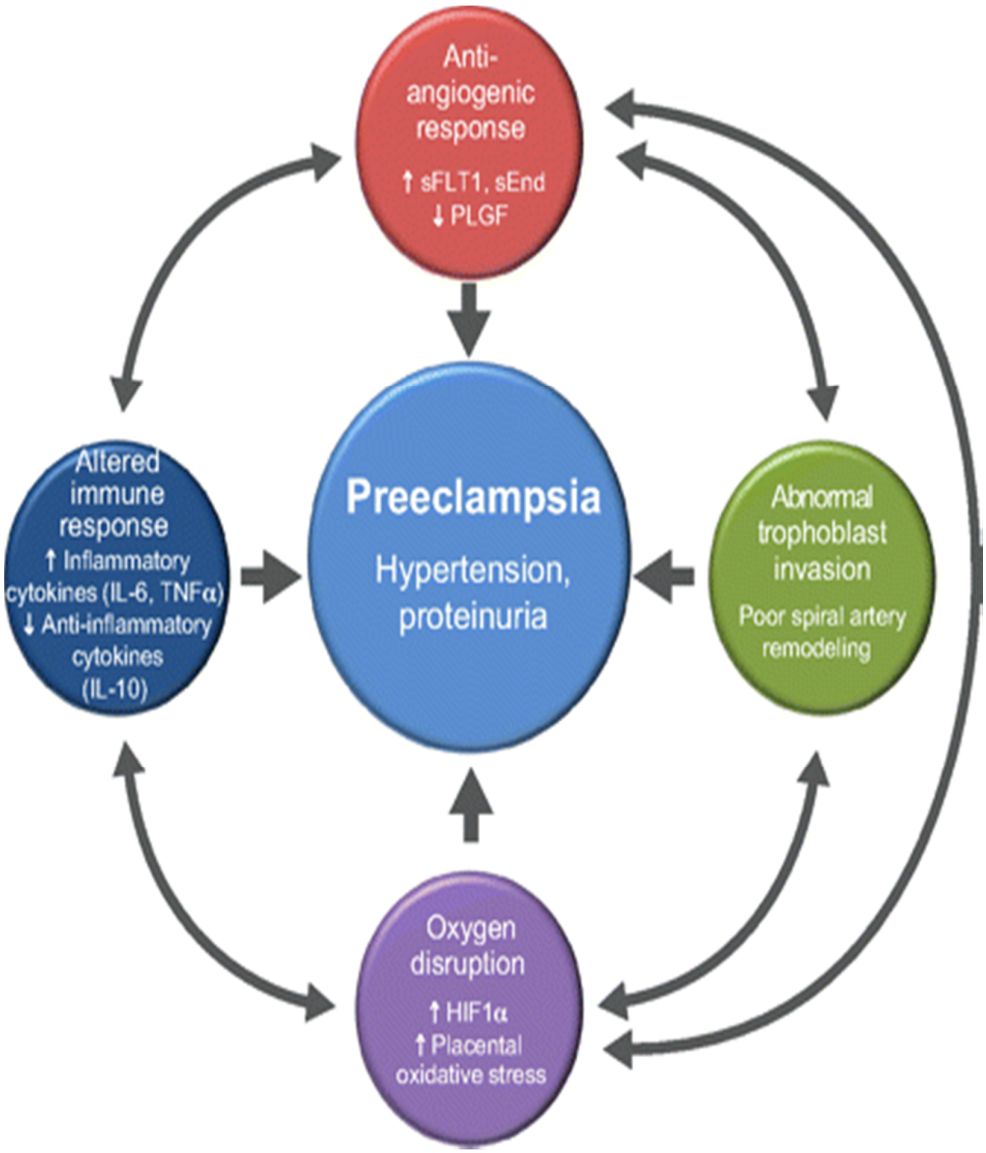
Proteinuria defined as urinary excretion of >150mg of protein / day over 24 hours of urine collection. It is due to increased permeability of glomerular capillaries to non filtered plasma macromolecules like albumin.

In a normal person the urinary protein excretion will be <150mg/day. Of which majority 60% consists of Albumin and 40% of tubular Tamm Horsfall Protein.

Proteinuria in pregnancy defined as excretion of urinary protein of >300mg/day in 24 hours urine collection.[29]

Inspite of all the above explanation, proteinuria in preeclampsia represents the severity of disease. The absence of it does not exclude the severe form of preeclampsia. From the reference reported that eclampsia and severe preeclampsia can occur without proteinuria.[30]

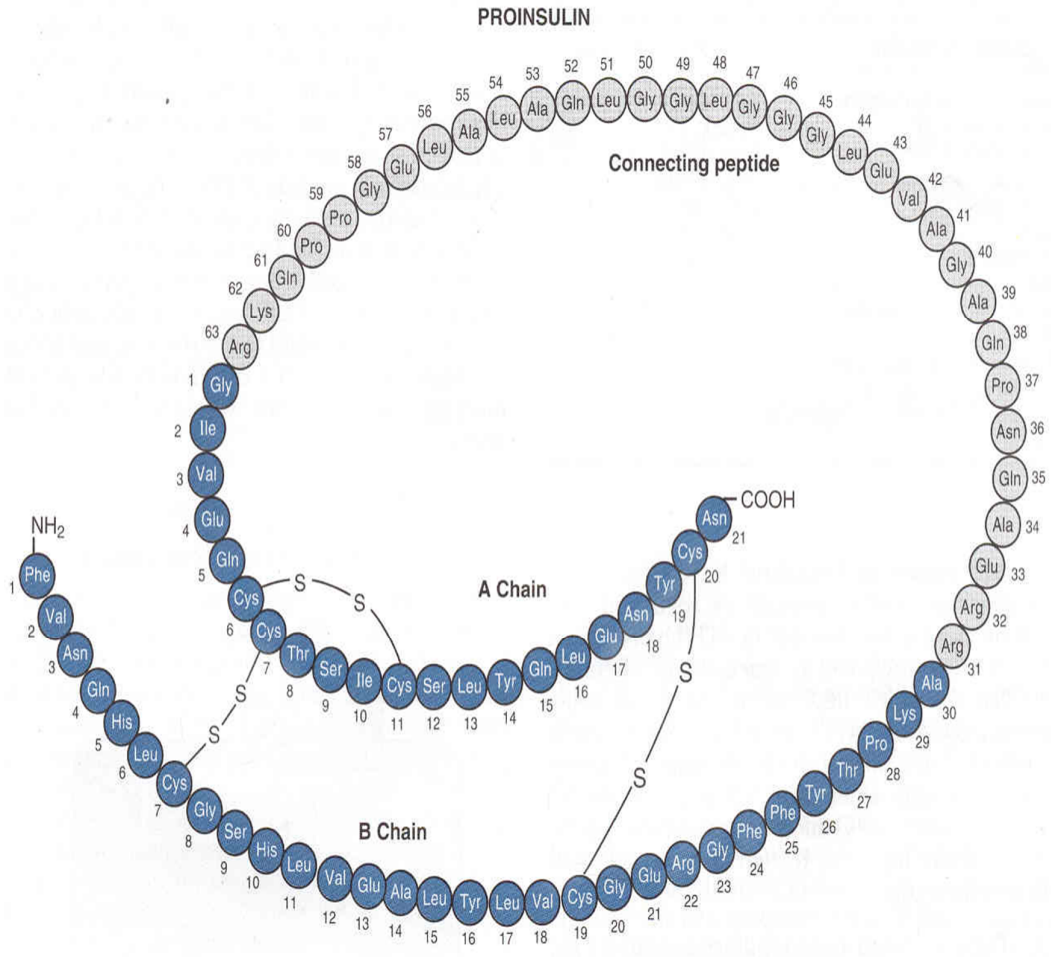
PROTEINURIA:



INSULIN:

In 1921 Frederick G.Banting and Charles H. Best successfully discovered the Insulin.

STRUCTURE



Insulin is a large polypeptide hormone consisting of two aminoacid (21AA and 30AA) linked by disulfide bonds. Insulin also known as hormone of nutrient abundance.

INSULIN SYNTHESIS:

Insulin gene encodes a large precursor of insulin known as preproinsulin, during translation, the signal peptide is cleared into proinsulin. While packaging in granules by Golgi this proinsulin is cleared into insulin and C-peptide.

DNA (Chromosine 11) in βcells

↓

mRNA

↓

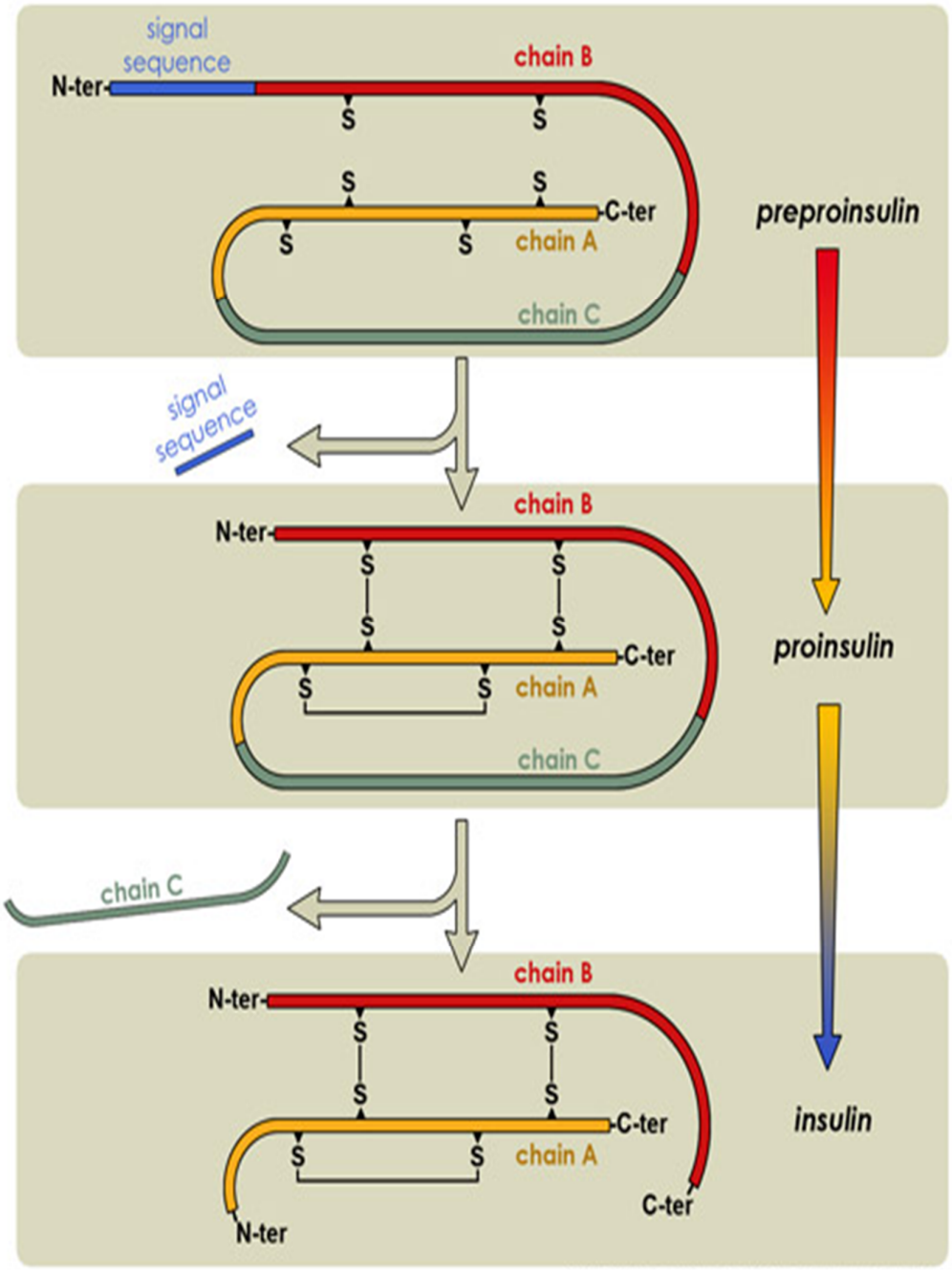
Preproinsulin (Signal peptide, A chain, B chain and Peptide C)

↓

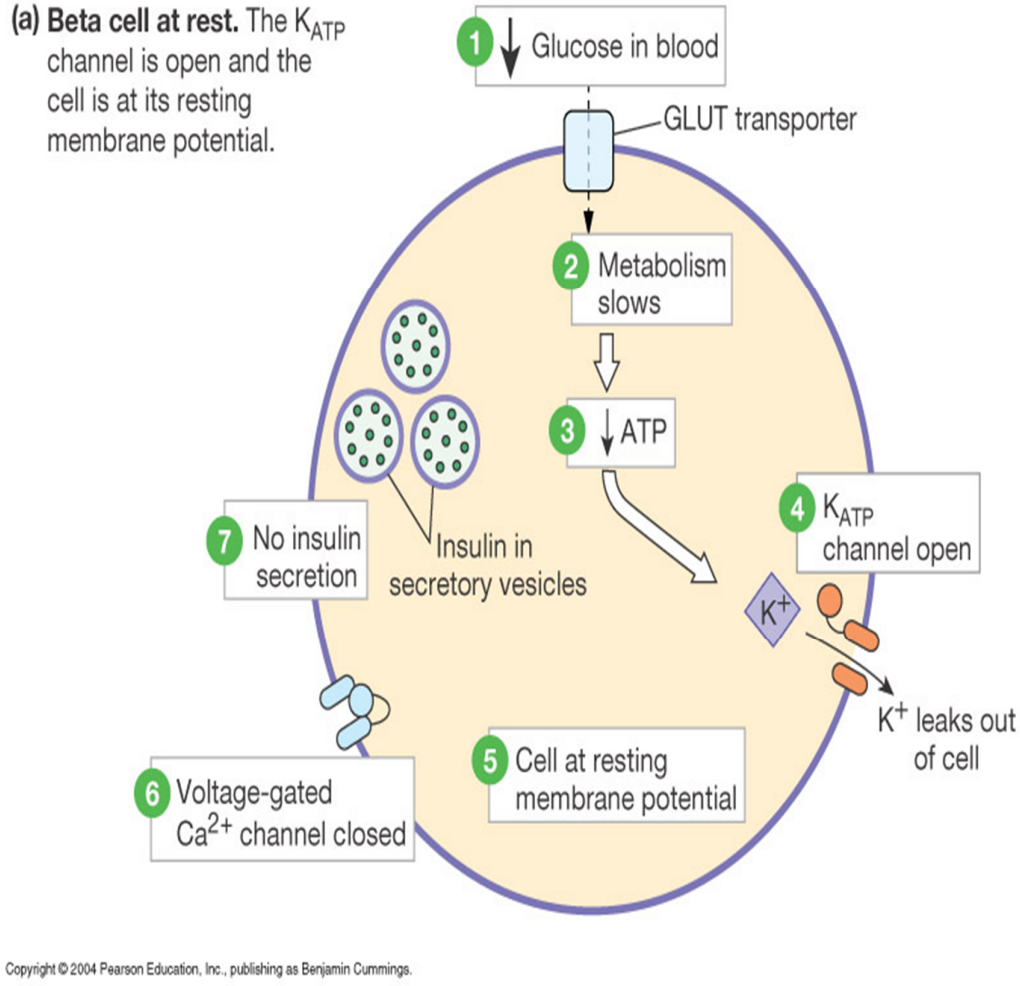
Proinsulin

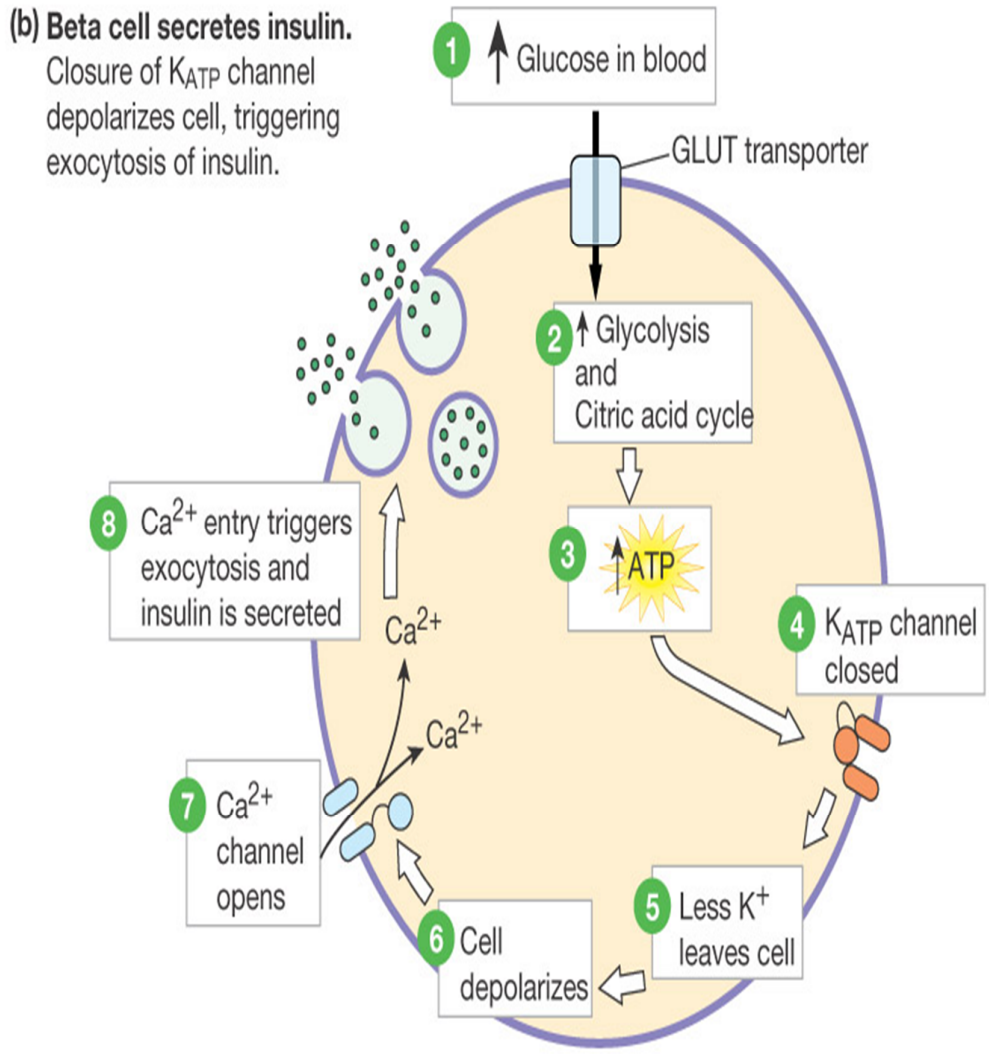
↓

Insulin


signal
sequence
chain B
N-ter
S
C-ter
chain A
chain C
preproinsulin
proinsulin
insulin

Metabolic regulation of insulin secretion:





Glucose entered into the β cells by Glut-2 carriers this action is

independent of the presence of insulin

↓

Phosphorylation of glucose by glucokinase

↓

Metabolisation with synthesis 0f ATP

↓

With increasing ATP closing of ATP dependent K^+ channels

↓

Ca2+ entry triggers exocytosis

↓

Secretion of insulin

REGULATION OF INSULIN SECRETION:

Regulators of Insulin Secretion	
Stimulators of Insulin Secretion	**Inhibitors of Insulin Secretion**
↑ Serum glucose ↑ Serum Aminoacids ↑ Serum free fatty acids ↑ Serum ketone bodies **Hormones:** • Gastro inhibitory peptide • Glucagon • Gastrin • Cholecystokinin (CCK) • Secretin • Vasoactive intestinal peptide (VIP) • Epinephrine (β receptor) **Parasympathetic nervous system**	↓ Glucose ↓ Aminoacid ↓ Free fatty acid **Hormones:** • Somatostatin • Epinephrine (α-receptor) Sympathetic nervous system stimulation

Reference – Valve for Insulin Levels

0.7-25μ units/ml

HYPERINSULINEMIA

Genetic Factor	Life Style Changes	Drugs	Pathological
• Ethinicities (American, Hispanic, African) • Family history with Type2 DM • Insulin receptor mutation (Donohue syndrome) • LMNA mutation (Familial partial lipodystrophy) • Gestational Diabetes Mellitus	• Increasing age • Stress • Sedentary life style • Lack of physical exercise • Obesity • Tobacco smoking • Caffine intake • Alcohol	• Corticosteroids • Progestogens • Rifampicin • Isoniazid • Olanzapine • Methadone • Anti retrovirals	• Metabolic syndrome • Liver pathologies • Infection (Hepatitis-C) • Haemochromatosis • Polycystic Ovarian Syndrome • Gastroparesis

Insulin Resistance and Normal Pregnancy:

Pregnancy is a diabetogenic state therefore there are high changes of metabolic instability of glycemic control can occur in pregnancy. However insulin resistance and the resultant hyperinsulinemia are characteristic of normal pregnancy and this will be maximal during third trimester. This could probably mediated by increasing amounts of several insulin antagonistic hormones including human placental lactogen,[1,2] progesterone[3] and corticotrophin[4] releasing hormone. As a result of this peripheral and hepatic insulin resistance develops by second trimester despite exaggerated maternal insulin response and increased maternal plasma insulin levels.

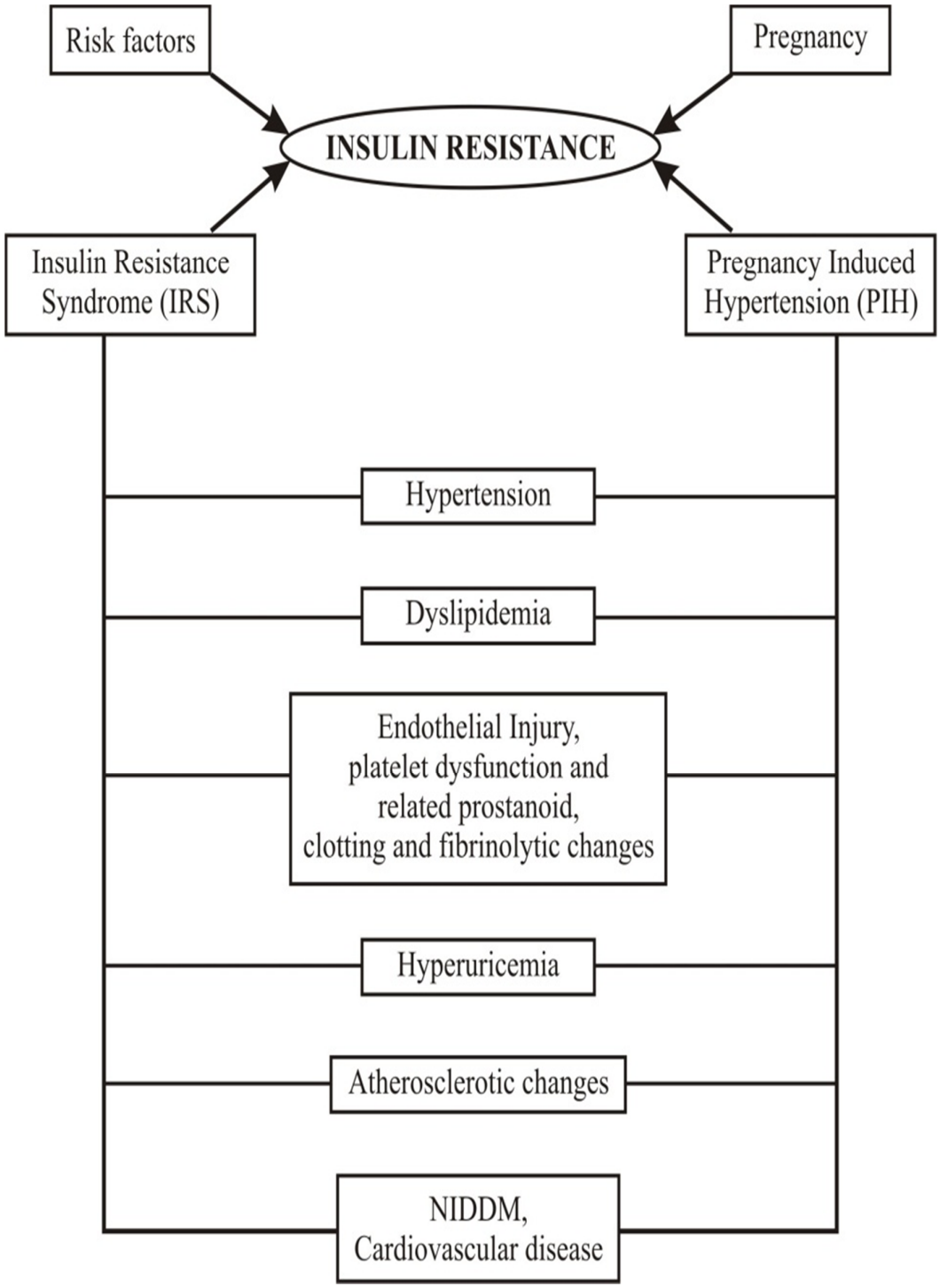
INSULIN RESISTANCE AND HYPERTENSIVE PREGNANCY:

In hypertension complicated pregnancies there will be an exaggeration of insulin resistance and the associated metabolic changes. Features of Insulin resistance accompanied by preeclampsia includes;

- Hypertension
- Obesity
- Lipid abnormalities
- Hyperinsulinemia
- Glucose intolerance

- Elevated testosterone
- Reduced sex hormone binding globulin

Evidence suggest that insulin resistance is intrinsically linked to high blood pressure.[31,35] The association between insulin resistance and hypertension was first reported in 1966 [36] and further enormous clinical and epidemiological studies have confirmed it.[33,37-50] These studies pointout that hypertensives tend to be more hyperinsulinemic in comparison to normotensive individuals. However the relationship between the insulin resistance and hypertension is independence of BMI, Age and magnitude of glucose tolerance.[51]


Risk factors
Pregnancy
INSULIN RESISTANCE
Insulin Resistance Syndrome (IRS)
Pregnancy Induced Hypertension (PIH)
Hypertension
Dyslipidemia
Endothelial Injury, platelet dysfunction and related prostanoid, clotting and fibrinolytic changes
Hyperuricemia
Atherosclerotic changes
NIDDM, Cardiovascular disease

There are several clinical, epidemiological and experimental data currently support not only an association but a causal link between insulin activity and blood pressure.[32,36,52-55]

Several datas have documented hyperinsulinemia in early and mid pregnancy before the development of preeclampsia. Exaggerated hyperinsulinemia when compared to normal pregnancy[56,57] is well explained in women with established preeclampsia.

Decreased levels of sex hormone binding globulin (SHBG) which is considered as a marker of hyperinsulinemia has been linked to increased incidence of development of preeclampsia complicating pregnancy. This is seen as early as 1st trimester.

Recent studies also indicate that women who had experience preeclampsia in their pregnancy may be at increased risk in later life for the development of complication associated with insulin resistance which include Type-2 Diabetes Mellitus, Hypertension. Dyslipidemia and cardiac diseases.

PREECLAMPSIA ASSOCIATED WITH HYPERINSULINEMIA

In the regulation of blood pressure, the role of insulin remains unclear, but several mechanism has been studied, they are

1. Stimulation of sympathetic nervous system
2. Retention of sodium
3. Endothelial dysfunction
4. Increases sensitivity to vasopressors
5. Enhance the cation transport
6. Defects in insulin action

1) Stimulation of sympathetic nervous system:

Pregnancy complicated by preeclampsia associated with insulin resistance and hyperinsulinemia can be understood by insulin activity on renal and cardiovascular system.

Hyperinsulinemia

↓

Stimulation of sympathetic system

↓

Increase in catecholamines concentration

↓

Increase in the peripheral vasoconstriction

↓

Elevation of blood pressure

2) Retention of sodium:[35,59]

There are several physiological actions of insulin that may either directly or indirectly affect the sodium and water balance, vascular resistance and cardiac contractility. In normal pregnancy there will be a tendency to retain sodium and this physiological phenomenon can be aggravated by insulin which is in excess in preeclampsia. Therefore insulin has been considered as a regulator of hypertension and an intensifier of physiological phenomenon in preeclamptic pregnancy.

3) Endothelial dysfunction:[17,18]

Hyperinsulinemia causes endothelial damage by several machanism, which is involved in the pathogenesis of preeclampsia.

Endothelial dysfunction

↓

Increase in the formation of endothelin thromboxane

↓

Increased vascular sensitivity to Angiotensin II and decreased formation of the vasodilators such as prostacyclin and nitric oxide.

4) Increases the Sensitivity to Vasopressors:[60-62]

In preeclampsia there is a defect in insulin action which leads to increased vascular tone and enhances the sensitivity to vasopressors such as angiotensin and other vasoconstrictor.

5) Enhance the cation transport:[32,63-66]

Several studies has been postulated that insulin may regulate intracellular calcium levels and modulate intracellular cation pumps, thereby affecting vascular tone and blood pressure.

6) Defects in the insulin action:[67-69]

There are several abnormalities in lipid metabolism especially, increased levels of triglyceride, FFA, very low density lipoprotein (VLDL), low density lipoproteins (LDL) and decreased levels of high density lipoproteins (HDL). These abnormalities has been strongly associated with development of preeclampsia.[67-69]

Compared to normal pregnancy, preeclampsia associated with hyperinsulinemia which is reflected by high fasting plasma insulin levels. It was postulated that hyperinsulinemia might contributes to the pathogenesis of preeclampsia.[80]

Bauman et al [22] was first reported the association between insulin levels and hypertension during pregnancy. They documented that hypertensive patients were more hyperinsulinemic compared to normotensive patients. The levels of hyperinsulinemia in preeclampsia were positively correlated with systolic and diastolic blood pressure.

In this regard "Paretti et al [81] documented that correlation of insulin resistance and the fasting insulin level using several insulin sensitivity tests will be useful in predicting the development of preeclampsia. There is an increased incidence of insulin resistance among women who subsequently developed preeclampsia. It postulates that insulin resistance might be in causal pathway of preeclampsia.

Solomon et al,[70] reported that higher fasting insulin and cholesterol levels in mid trimester are frequently associated with high risk for developing pregnancy induced hypertension and study revealed the role of insulin resistance in the development of complications during pregnancy.

Defronzo[71] documented that the association between hyperinsulinemia and hypertension and the study suggested that insulin plays a pivotal role in hypertension observed often in obese subjects through its direct effect on the renal sodium retention.

Kaplan[74] indicated that hyperinsulinemia and insulin resistance has a important role in pathogenesis of preeclampsia.

Feldman and Bierbrier [72] recently reported that insulin acts as a direct vasodilator and they demonstrated the vascular sensitivity to insulin similar to the systemic metabolic sensitivity which was decreased in hypertensive patients.

Preeclampsia, a pregnancy specific syndrome is known to accompanied by metabolic changes similar to insulin resistance syndrome.

Kaaja et al [73] reported more recently that women with preeclampsia are more hyperinsulinemic than normotensive controls.

Reaven et al[31] indicated that hyperinsulinemia and insulin resistance may play a vital role in the pathogenesis of syndrome X, which is characterized by hyperinsulinemia, insulin resistance, increased levels of VLDL, glucose intolerance and hypertension.

Rowe et al[58] found that insulin increases the blood pressure by increasing the sympathetic tone.

Laivori et al[57] suggested that higher fasting insulin levels among 22 women with preeclampsia comlicated pregnancy as compared with normotensive pregnancy.

Fuh et al[56] documented in their study that 13 women with preeclampsia complicating pregnancy 13 women with normotensive pregnancy and 8 weeks postpartum found high insulin levels in the group with the history of preeclampsia.

Sowers et al[75] reported in its prospective study of 164 predominantly black women, he noted significantly higher insulin levels among women, subsequently developing pregnancy induced hypertension as compared to normotensive controls.

Wolf et al indicated that lower sex hormone binding globulin in first trimester correlated negatively with insulin resistance and hyperinsulinemia in women subsequently developing preeclampsia as compared with normotensive pregnancy.

Lasko [82] found that fasting insulin levels used as a marker of insulin resistance.

Modan et al[84] conducted a large epidemiological study and found a strong association between hyperinsulinemia, hypertension and impaired

GTT in a random population sample. Several studies conducted recently have documented that preeclamptic women, have insulin resistance for months after delivery.

Some of the cross sectional studies suggested that women with established preeclampsia having higher fasting insulin [75,76] levels and low insulin sensitivity than the controls. All together these data indicated that insulin resistance may contribute to the pathogenesis of preeclampsia.

Certain studies documented that women with preeclampsia had higher fasting insulin level at their second trimester, even before the appearance of clinical signs of preeclampsia.[70,75,76,78]

In a prospective study conducted on nulliparous women reported that an association between the sex hormone binding globulin and preeclampsia and the study was strengthened among the lean women with increased level of SHBG associated with marked decrease in the risk of developing preeclampsia.

Plasma insulin level in a fasting state are measured by using a double antibody radioimmunoassay.[85]

Materials and Methods

MATERIALS AND METHODS

Sample Size:

Hundred pregnant women (70 cases and 30 controls) admitted to Institute of Obstetrics and Gynaecology, Madras Medical College during the study period (September 2014 to July 2015) was enrolled for the study, who satisfied the inclusion criteria.

Study type:

Comparative Study

Period of Study:

10 Months

Method of collection of data:

A comparative study was conducted on 100 pregnant women in their 3rd trimester who were enrolled in the study based upon the fasting insulin level and their correlation with the severity of the disease based on their age, parity, gestational age and severity of hypertension was studied.

After obtaining all proper consent for the study, all the women were subjected to detailed history, examination and all were verified for the use of iron, folic acid, vitamins and any other drugs.

Besides all routine antenatal investigations and special investigations in preeclamptic women all of them were subjected to fasting plasma insulin levels.

Fasting plasma insulin level was measured by taking 3ml of blood from the antecubital vein in the fasting state after overnight all the blood specimens were transported to the laboratory within 2 hours of collection. Then the specimens were centrifuged for 6-8 minutes at 2000rpm. Clear serum separated which was stored in a refrigerator until analysis. Thereafter the samples were subjected to Chemiluminescent Immunoassay (CLIA) technique using the FDA approved reagent and kit.

DATA ANALYSIS:

Statistical analysis of the collected data was done by;

- Pearson chi-square test
- Fischer's test
- 't' test

$p<0.05$ was taken as statistically significant

INCLUSION CRITERIA:

After the written and informed consent, pregnant women with preeclampsia taken as cases and normotensive pregnant women taken as control group all antenatal pregnant women between 26-38 weeks.

- Hypertensives (cases)
- Normotensives (control)

EXCLUSION CRITERIA:

- Diabetes mellitus
- Chronic hypertension
- Renal disorder
- Liver disorder
- Coagulopathy
- Collagen vascular disorder
- Neural tube defect

Results

RESULTS & ANALYSIS

Table 1 : Number of women in the study

Group	Number
Preeclampsia	70
Normotensive	30
Total	100

The current study was conducted on 100 women of which 70 preeclampsia women were taken as cases, 30 normotensive were taken as control.

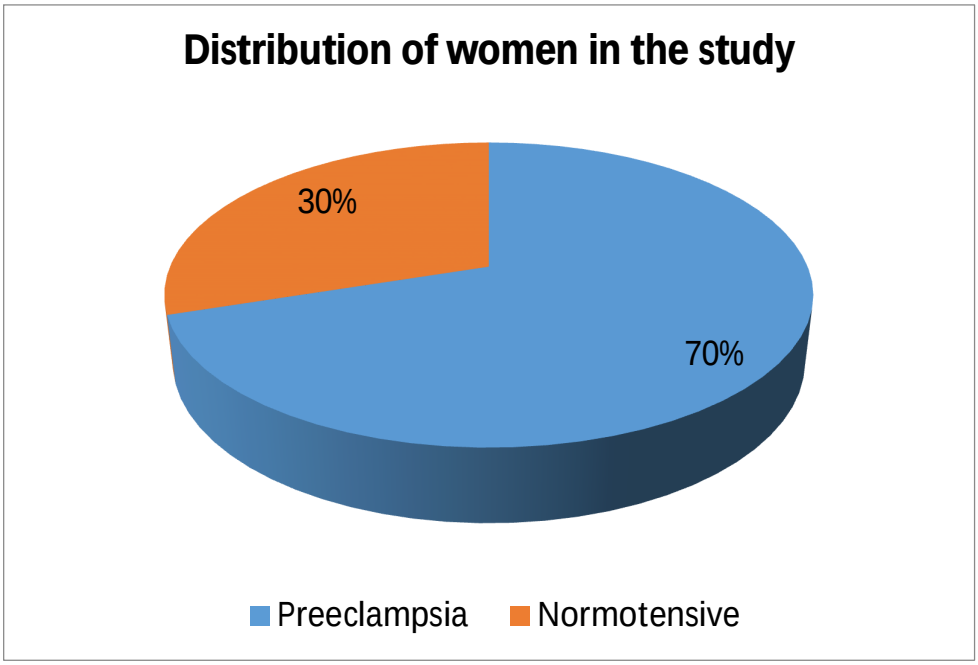


Table 2: Severity of Hypertension

Group	No	%
Mild Preeclampsia	24	34.3%
Severe Preeclampsia	46	65.7%
Total	70	100%

Based on NHBPEP 2000 classification the cases were further classified into mild and severe preeclampsia. Among the cases in the study 34.3% (24) were in mild preeclampsia, 65.7% (46) were in severe preeclampsia.

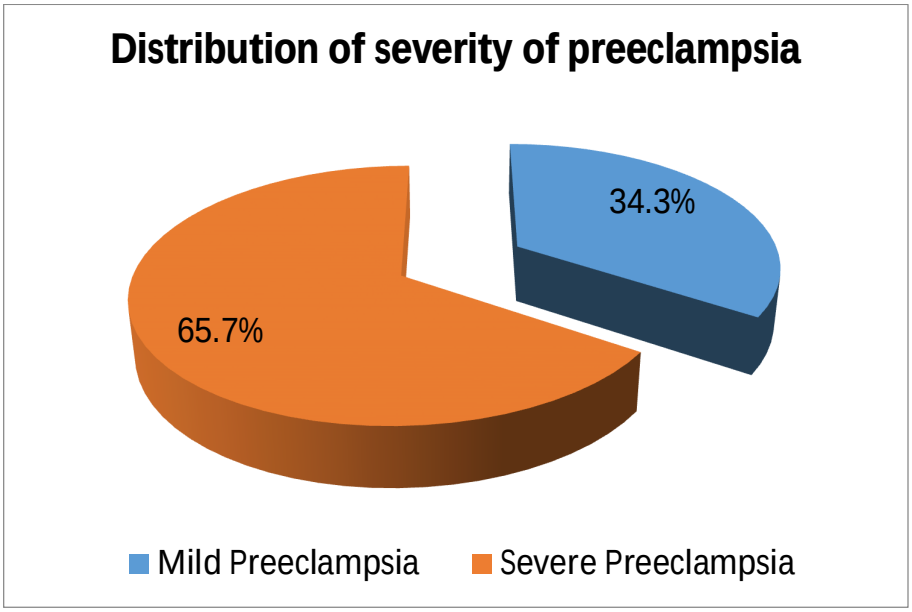


Table 3 : Age Distribution

Age		< 20 Yrs	20-30 yrs	>30 yrs	Total
Control	No	5	17	8	30
	%	45.5%	26.2%	33.3%	30
Mild	No	3	19	2	24
	%	27.3%	29.2%	8.3%	24
Severe	No	3	29	14	46
	%	27.3%	44.6%	58.3%	46
Total	No	11	65	24	100

$X^2 = 3.073$ p = 0.215 NS

The mean age of the women in the control group was 26.17 and in study group was 27.09 which was comparable with both groups. In this study maximum number of women were in the age group between 20-30 years (65%) in control and study group. The results obtained were statistically not significant.

Table 4 : Patient Profile

	Age	Parity	Gestational Age	BMI
Control Group N=30	26.17 (18-40 yrs)	Primi 50% Multi 50%	35.17% (26-38 wks)	24.53
Study Group N=70	27.09 (18-40 yrs)	Primi 71.4% Multi 28.6%	33.41% (26-38 wks)	24.83

Table 5 : Parity Distribution

Parity		Group		Total
		Control	Study	
Primi	Count	15	50	65
	%	50%	71.4%	65%
Multi	Count	15	20	35
	%	50%	28.6%	35%
Total	Count	30	70	100
	%	100%	100%	100%

$X^2 = 6.992$ P=0.030HS

In control group, number of primigravida was 50% and 71.4% in the study group, where as the multi's were 50% in the control group and 28.6% in study group and the results obtained were statistically significant.

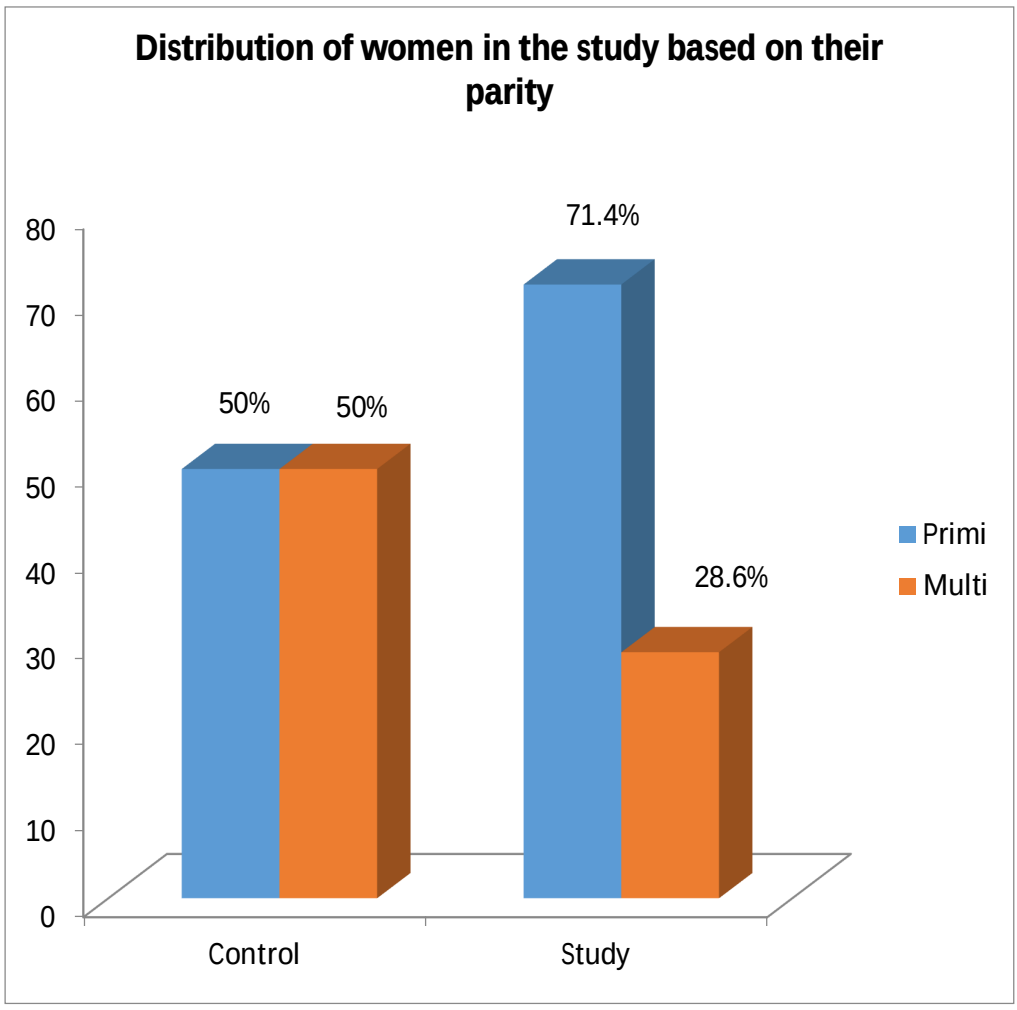


Table 6 : Period of Gestation at the time of sampling

Group	26-32 wks	33-38 wks
Control	5 (16.7%)	25 (83.3%)
Mild	10 (14.3%)	14 (20%)
Severe	20 (28.6%)	26 (37.1%)

Fishers exact test p = 0.008 HS

83.3% women in control group, 57.1% with variable degree of preeclampsia were at late trimester at the time of sampling.

16.7% of women in control and 42.9% of women with preeclampsia were at early gestation at the time of sampling. As per statistical analysis the period of gestation shows significance.

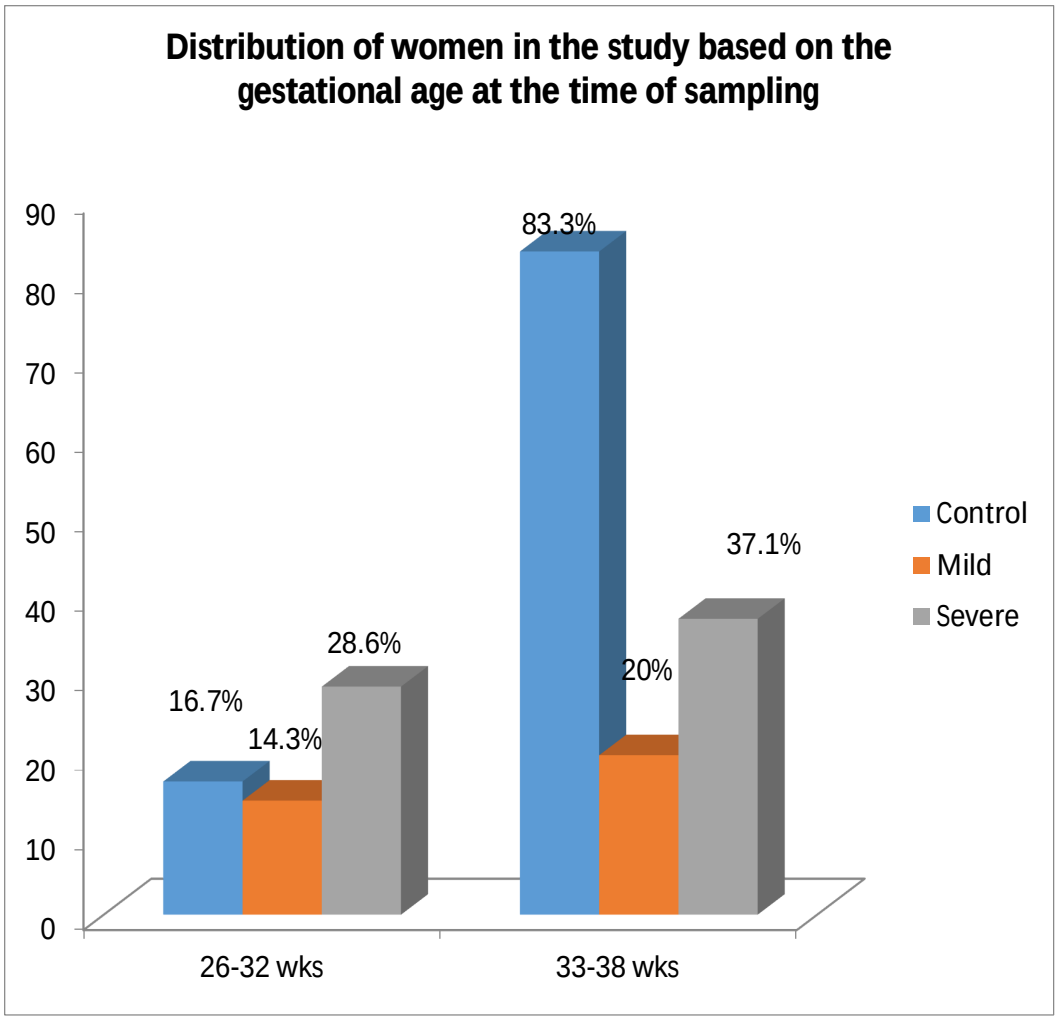
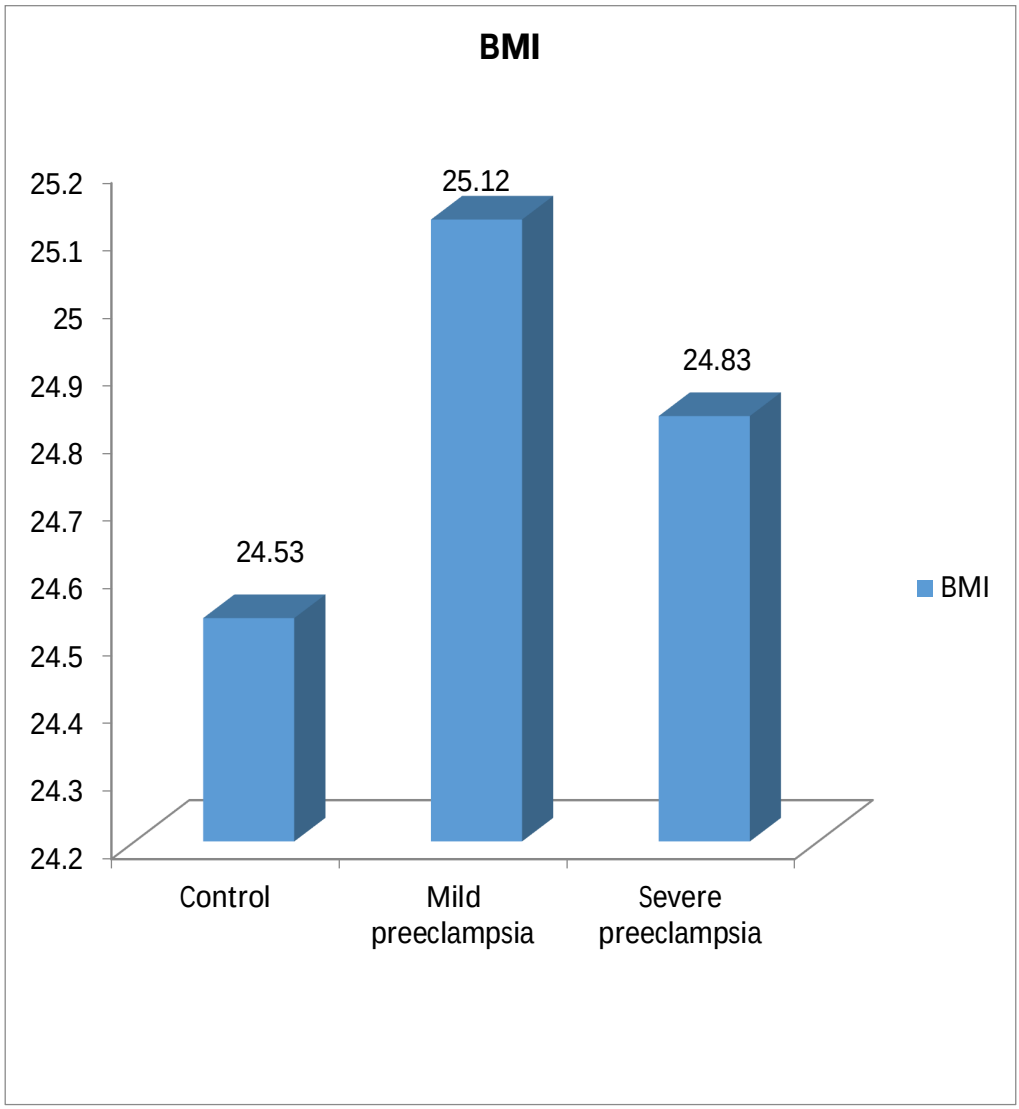

Distribution of women in the study based on the gestational age at the time of sampling
90
80
70
60
50
40
30
20
10
0
16.7%
14.3%
28.6%
83.3%
20%
37.1%
26-32 wks
33-38 wks
Control
Mild
Severe

Table 7 : BMI

	No	**Mean BMI**	**SD**
Normotensive	30	24.53	2.83
Mild preeclampsia	24	25.12	2.78
Severe preeclampsia	46	24.83	2.68

F=0.316 P=0.575 NS

The mean BMI in the normotensive group was 24.5 and in mild preeclampsia, severe preeclampsia was 25.12, 24.83 respectively. BMI was slightly more in preeclampsia group, possibly due to edema.

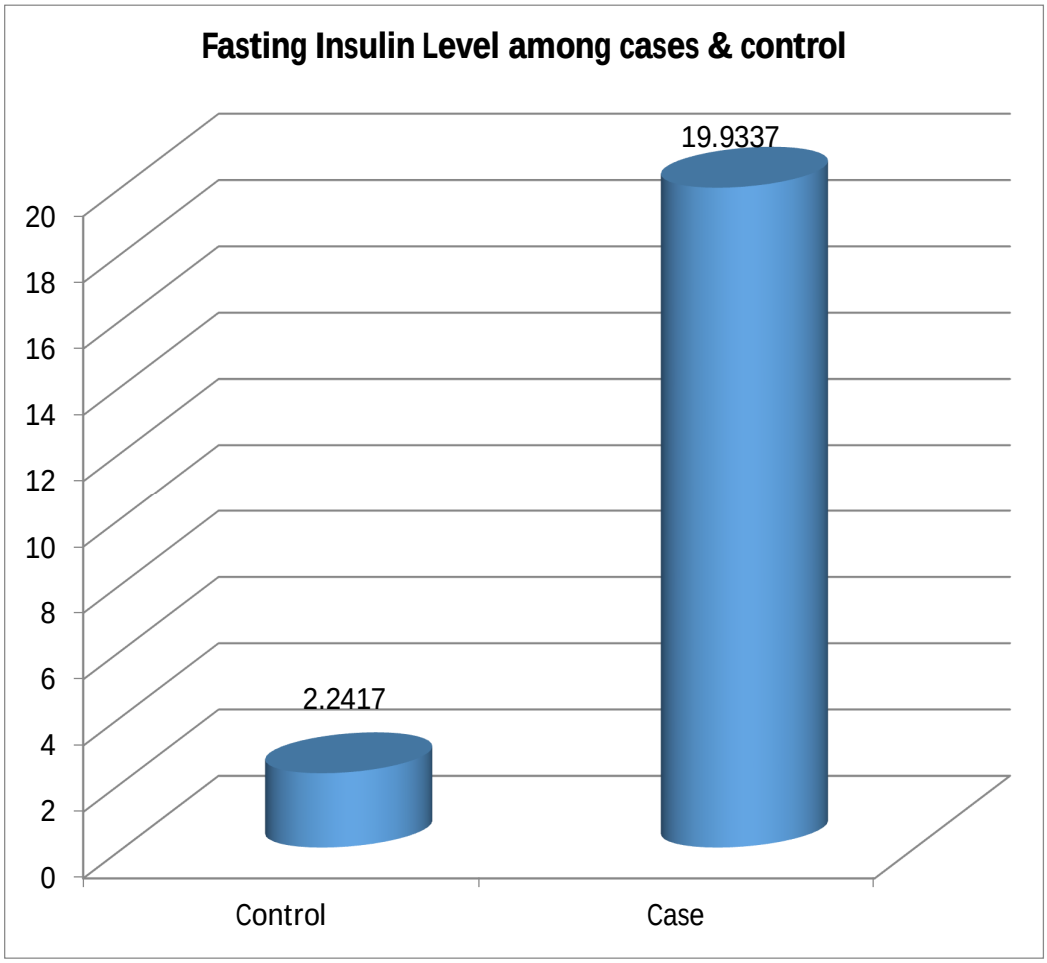


Distribution of women in the study based on BMI

Table 8 : Fasting insulin level among cases and control

	N	Mean	SD	SE
Normotensive	30	2.2417	1.84956	0.33768
Preeclampsia	70	19.9337	11.62100	1.38898

F=164.516 P=0.000 VHS

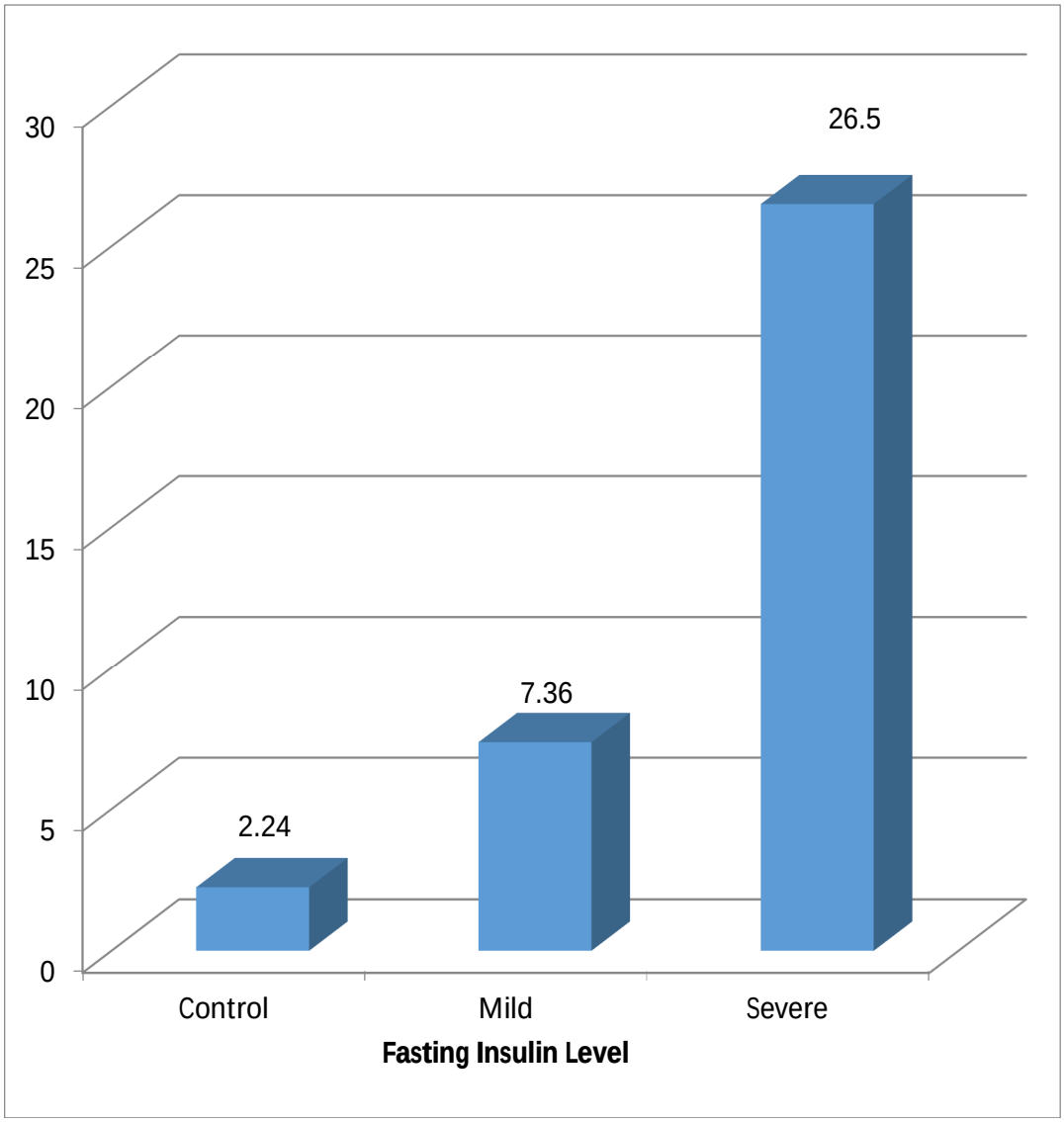


In the present study, the mean fasting insulin levels in normotensive group was 2.24µunit/ml and in preeclampsia group was 19.9337µunit/ml. The results obtained indicates that fasting insulin levels were high in preeclampsia study group as compared to the normotensive control group and the results were statistically significant, p=0.000 vhs.

Table 9 : Fasting Insulin Level in Various groups

	N	Mean	SD
Normotensive	30	2.2417	1.84956
Mild preeclampsia	24	7.3571	2.30602
Severe preeclampsia	46	26.4954	8.71688

F=164.516; p=<0.000



Distribution of the fasting insulin level among controls and various groups of preeclampsia

The mean fasting insulin level in control group were 2.24 µunits/ml, in mild preeclampsia was 7.36 µunits/ml, in severe preeclampsia it was 26.50 µunits/ml. However all two groups of cases had higher values of fasting insulin levels as compared to normotensives (2.24µunits/ml) and difference among each group were statistically significant with P=0.000 vhs.

Discussion

DISCUSSION

Preeclampsia is a pregnancy specific syndrome which is leading cause of maternal and fetal morbidity and mortality. However the exact pathogenesis of preeclampsia is still unknown, we have considered that in preeclampsia the basic pathophysiology is endothelial dysfunction and generalized vasospasm.

Hyperinsulinemia has been considered as a risk factor for peripheral vascular disorder and coronary heart disease. This risk is due to the modification of endothelial function as result of exposure to high insulin level.

Although the exact mechanism by which insulin causes endothelial dysfunction remains uncertain, but it appears to involve both cytotoxic and oxidative stress mechanism is very similar to those hypothesized to promote endothelial dysfunction in preeclampsia. However the pathogenesis of preeclampsia sharing striking similarities to that of artherosclerosis. So that it has been postulated that insulin concentration is greater in preeclampsia patient when compared to normotensive pregnant patients.

Study	Normotensive µunits/ml	Preeclampsia µunits/ml	P value
Hamaski T et al (1996)	7.3 n=551	24.1 n=29	P<0.05
Soloman et al (1999)	7.9 n=551	13.3 n=29	P=0.03
Chandana Tripathy et al (1999)	6.33 ± 2.83 n=551	9 ± 5 n=29	P=0.0004
Shohreh et al (2002)	16.2 ± 1.3 n=16	25.3 ± 1.4 n=16	P<0.01
Lei Q et al (2008)	8.92 ± 4.4 n=200	11.44 ± 6.72 n=33	P=0.005
Present Study (2014)	2.24 n=30	19.9337 n=70	P<0.000 vhs

In our present study, we have compared the fasting plasma insulin levels among the preeclamptic women and the normotensive pregnant women.

This study represent that, the mean value of fasting plasma insulin levels among normotensive group was 2.24 µunits/ml and preeclamptic group was 19.9337µunits/ml and the results were comparable with that of studies by Chandana Tripathy et al, Shoreh et al, Lei Q et al, Solomon et al., as seen in the above table.

There was a study conducted by Hamaski T et al [88] on 551 normotensives and 29 preeclamptic women with fasting plasma insulin values of 7.3 µunits/ml vs 24.1µunits/ml respectively which was comparable with the results of our present study.

Soloman et al[70] conducted study on 31 normotensive and 31 preeclamptic women with fasting plasma insulin levels of 7.9 µ units/ml vs 13.3 µ units/ml respectively. P value of this study was 0.03, statistically significant.

Furthermore another study was performed by Chandana Tripathy et al was done among 99 normotensive and 104 preeclamptic women with fasting insulin levels as follows;

Control Group = 6.33 $\pm$ 2.83 µunits / ml (n=99)

Study Group = 9 $\pm$ 5 µunits(n=104)

P = 0.0004 statistically significant.

Shohreh et al [86] performed the study on 16 normotensive and 16 preeclampsia women. The result in the preeclampsia women were higher 25.3 $\pm$ 1.4 µunits/ml when compared to normotensive pregnant women with fasting insulin value of 16.2 ± 13 µunits / ml; p=<0.01.

According to Lei Q et al, study performed on 200 normotensive pregnant women and 33 preeclamptic women with fasting insulin value of 8.92 $\pm$ 4.4µunits/ml vs 11.44 $\pm$ 6.72 µunits/ml respectively, p=0.005.

Another study performed by Roberts et al [39] showed that the fasting insulin levels among 11 normotensive and 11 preeclamptic women and the results were not comparable with hypothesis. The mean fasting insulin level was significantly lower in preeclamptic women when compared to control group i.e. 10mu/L vs 16.6 mu/L, p=0.016, here the study showed that preeclampsia was not correlated with an elevated insulin resistance beyond that of normal pregnancy, mutually the reverse is true.

To conclude, the fasting insulin levels are elevated in preeclampsia as compared to normotensive pregnancy and this was emphasized in the present study with the supportive results.

The fasting plasma insulin levels in control, mild, severe pre eclampsia were 2.2417 µunits/ml, 7.3571 µunits/ml and 26.4954 µunits/ml with p value of <0.000 vhs. The results were statistically significant.

The mean age of control group was 26.17 and study group was 27.09 which was statistically not significant.

The mean gestational age of control group and study group was 35.17 and 34.1 respectively which was statistically significant.

The mean BMI in the normotensive group was 24.5 and in mild preeclampsia, severe preeclampsia was 25.12, 24.83 respectively. BMI was likely more in preeclampsia group, possibly due to edema. BMI was not statistically significant.

However there were no studies compared the severity of the disease with fasting plasma insulin values, significant positive correlation was detected among the several studies conducted showing a higher fasting insulin levels among the preeclamptic women on compared to normotensive pregnant women with p values being statistically significant.

Summary

SUMMARY

The present study was a prospective comparable study performed to determine fasting plasma insulin levels in normotensive pregnant women and the preeclamptic women and their relationship with the severity of the disorder.

Among 100 pregnant women, 30 were normotensives and 24 were mild preeclamptic, 46 were severe preeclamptic.

The mean age of control group was 26.17 and study group was 27.09.

The mean gestational age of control group and study group was 35.17 and 34.1 respectively.

The mean fasting insulin level of control, mild and severe preeclampsia was 2.2417µunits/ml, 7.3571µunits/ml and 26.4954µunits/ml respectively with p value of 0.000vhs, which was significantly elevated as compared to normotensive group.

The elevated fasting plasma insulin was appears to be directly proportional to the severity of the disease. According to the values of mild preeclampsia (7.357 µunits/ml) and severe preeclampsia (26.4954 µunits/ml) the later group was having higher fasting insulin value when compared to mild preeclampsia.

Conclusion

CONCLUSION

The present study states that pregnancy complicated by preeclampsia tend to be more hyperinsulinemic when compared to normotensive pregnant women and the study emphasized that the relationship between hypertension and insulin resistance is independent of Age, BMI. By this study we enlighten that parity, and period of gestation showed statistical significance.

The present study, enlighten that fasting insulin level was elevated in preeclamptic women when compared to normotensive pregnant women. In addition to that it also represent the elevated fasting insulin levels were directly proportional to the severity of the disease.

Recommendation

RECOMMENDATION

Future studies needed in preeclamptic women about the cause of hyperinsulinemia which helps to improve the outcome of preeclamptic pregnant women.

Bibliography

BIBLIOGRAPHY

1. Reece EA, Homko C, Wiznitzer A. Metabolic changes in diabetic and nondiabetic subjects during pregnancy .Obstet Gynecol Survey 1994; 49(1): 64-71.
2. Carpenter MW. Metabolic changes in gestational diabetes. Clin Perinatol 1993; 20(3):583-91.
3. Ryan E, Enns L. Role of gestational hormones in the induction of insulin resistance. J Clin Endocrinol Metab 1991; 67(2):341-7.
4. Laatikainen T, Virtanen T, Kaaja R, Salminen - Lappalainen K. Corticotropin - releasing hormone in maternal and cord plasma in pre-eclampsia. Eur J Obstet Gynaecol Rcprod Biol 1991; 39(1): 19-24.
5. Chesley LC, The variability of proteinuria in the hypertensive complications of pregnancy. J. Clin Invest 1939; 18: 617-20.
6. Chesley LC, Markovitz I, Wetchler BB. Proteinuria following momentary Vasoconstriction J Clin Invest 1939; 18: 51-8.
7. Kyle PM, Fielder JN, Pullar B et al. Comparison of methods to identify significant prorinuria in pregnancy in the outpatient settings. Br. J. Obstet Gynecol 2008; 115:523.
8. Report of the National High Blood Pressure Education Programme Working Group on High Blood Pressure in Pregnancy. Am J Obstet Gynecol 2000; 183: 51-2.
9. Cunningham FG, Leveno KJ, Bloom SL, Hauth JC, Rouse DJ, Spong CY. Williams Obstetrics 23rd ed McGraw - Hill Medical Publishing Division; 2010. P. 706-56.
10. Wagner LK : Diagnosis and management of pre-eclampsia. Am Fam Physician, 2004; 70: 2317-24.
11. Vinatier D, Monnier JC. Pre-eclampsia: physiology and immunological aspects. Eur J Obstet Gynecol Rcprod Biol 1995; 61(2):85-97

12. Cooper DW, Brennecke SP, Wilton AN. Genetics of pre-eclampsia. Hypertens Prcg 1993; 12(1): 1-23.

13. Handwerker SM, Altura BT, Altura BM. Ionized magnesium and calcium levels in umbilical cord serum of pregnancy women with transient hypertension during labor. Am J Hypertens 1993; 6(6, Part 1): 542-5.

14. Newman JC, Amarasingham. The pathogenesis of eclampsia: The "magnesium ischaemia" hypothesis. Med Hypotheses 1992; 40: 250-66.

15. Lalau JD, Jans I, el Esper N, Bouillon R, Fournier A. Calcium metabolism, plasma parathyroid hormone and calcitriol in transient hypertension of pregnancy. Am J Hypertens 1993; 6(6 pt 1): 522-7.

16. Williams MA, Zinghcim RW, King IB, Zebelman AM. Omega - 3 fatty acids in maternal erythrocytes and risk of preeclampsia. Epidemiology 1995; 6 (3): 232-7.

17. Cunningham, Gray F, Norman F. Gant, Kenneth J. Leveno et al, Williams Obstetrics, McGraw - Hill Medical Publishing Divisions, International edition, 2001; 21^{s1} edition, 568-618.

18. Clinical Obstctcrics and Gynaecology, Vol. 35, No. 2, June 1992, 338-47.

19. Myatt L, Brewer AS, Langdon G,Brockman DE: Attenuation of the vasoconstrictor effects and endothelin by nitric oxide in the human placental circulation Am J Obstet Gynecol, 1992,vol 166:224

20. Weincr CP, Thompson LP, Liu KZ, Herrig JE:Endothelium derived relaxing factor and indomethacin sensitive contracting factor alter arterial contractile responses to thromboxane during pregnancy. Am J Obstet Gynecol, 1992.vol 166:1171

21. Moris NH ,Eaton BM, Dekker G:Nitric oxide, the endothelium , pregnancy and pre eclampsia.Br J Obstet Gynecol,1996,voll03;4

22. Bauman WA, Maeimcn M, Langero O: An association between hypcrinsulinemia and hypertension during 3rd trimester of pregnancy. Am J Obstet Gnyccol. 1988; 159: 446-50.

23. Walsh SW: Pre-eclampsia: An Imbalance in placental prostacyclin and thromboxane production, Am J Obstet Gynecol, 1985, Vol 152: 335.

24. Nova A, Sibai BM, Barton JR et al: Maternal Plasma level of Endothclin is increased in Pre-eclampsia. Am J Obstet Gynecol, 1991, Vol 165: 724.

25. Faas MM, Schuiling GA, Liuton EA et al: Activation of peripheral leucocytes in late pregnancy and experimental pre-eclampsia Am J Obstet Gynecol, 2000, Vol 182:351.

26. Staff AC, Ranhein T, Khoury J, Henriksen T : Increased contents of phospholipids, cholesterol and lipid peroxides in decidua basalis in women with pre-eclampsia. Am J obstet Gynecol, 1999, vol 180:587.

27. Dizon - Townson DS et al: The factor V Leiden Mutation may predispose women to severe pre eclampsia. Am J Obstet Gynecol, 1996; Vol. 175: 902.

28. Groffrey Chaimberlain, Philip J Steer. 2001, Turnbull's obstetrics, 3rd edition. Churchill Liv ingstone.

29. Dennis A Daveyjan Mac Gillivray "The classification and definitionof hypertensive disorders of pregnancy".Am J Obstet Gynecol,1988,vol 158 :829-98

30. Sibai et al. Eclampsia: Observation from 67 recent cases, Obstet Gynecol, 1981;Vol 155: 1011-16.

31. Reaven GM. Role of insulin resistance in human disease. Diabetes 1988:37:1495-607.

32. Sowers JR, Sowers PS, Peuler JD. Role of insulin resistance and hypcrinsulinemia in the development of hypertension and atherosclerosis. J Lab Clin Med 1994; 123: 647-52.

33. Ferrannini E, Buzzigoli G, Bonnadonna R et al. Insulin resistance in essential hypertension. N Engl J Med 1987; 317: 350-7.

34. Jeng J-R, Sheu W-H, Jeng C-Y, Huang S-H, Shich S-M. Impaired fibrinolysis and insulin resistance in patients with hypertension. Am J Hypcrtens 1996; 9: 484-90.

35. Bhanot S, McNeill J. Insulin and hypertension: a causal relationship? Cardiovasc Res 1996;31:212-21.

36. Wellborn TA, Breckenridge A, Rubinstein AH et al. Serum insulin in essential hypertension and in peripheral vascular disease. Lancet 1996; 1: 1336-7.

37. Schmidt M, Watson R, Duncan R, Mctcaff P, Brancattik FL, Sharrett R et al. Clustering of dyslipidemia, hyperuricemia, diabetes and hypertension and its association with fasting insulin and central and overall obesity in a general population. Metabolism 1996; 45(6):699-706.

38. Berglund G, Larsson B, Anderson O, Larsson O, Svardsudd K, Bjortorp P et al. Body composition and glucose metabolism in hypertensive middle - aged males. Acta Med Scand 1976; 200: 163-9.

39. Robert RN, Haddeh DR. Insulin sensitivity pre-eclampsia, BJOG 2005; Vol. 105(10): 1095-100.

40. Lucas C, Estigarribia J. Darga L, Reaven G. Insulin and blood pressure in obesity. Hypertension 1985; 7: 702-6.

41. Singer P, Godicke W, Vioght S. Hajdu I, Weiss M. Postprandial hyperinsulinemia in patients with mild essential hypertension. Hypertension 1985; 7:182-6.

42. Ferrari P, Weidmann P. Insulin, insulin sensitivity and hypertension. J Hypertens 1990; 8: 491-500.

43. Ferrannini E, Haffner S, Stern M. Essential hypertension : an insulin-resistant state. J Cardiovasc Pharmacol 1990; 15 (Suppl 5): S18-S25.

44. Reaven GM. Relationship between insulin resistance and hypertension. Diabetes Care 1991; 14:33-8.

45. Faulkner B, Hulman S, Tannebaum J et al. Insulin resistance and blood pressure in young black men. Hypertension in young adult blacks. Hypertension 1993; 22-18-25.

46. Iimura O. Insulin resistance and hypertension in Japanese. Hypertens Res 1996; 19 (Suppl 1)S 1-8.

47. Van Minh H, Thanh L, Thi B, do Trinh T, Tho T, Valensi P. Insulinacmia and slight overweight: the case of Vietnamese hypertensives. Int J Obes Relat Metab Disord 1997; 21(10): 897-902.

48. Lender D, Arauz- Pacheco C, Adams - Huet B, Raskin P. Essential hypertension is associated with decreased insulin clearance and insulin resistance. Hypertension 1997: 29(1, Pt 1): 111-14.

49. Donahue R, Bean J, Donahue R, Goldberg R, Prineas R: Does insulin resistance unite the separate components of the insulin resistance syndrome? Evidence from the Miai Community Health Study. Arterioscler Thromb Vase Biol 1997; 17(11): 2413-17.

50. Mgonda Y, Ramaiya K, Swai A, McLarty D, Alberti K. Insulin resistance and hypertension in non-obese Africans in Tanzania. Hypertension 1998; 31(1): 114-18.

51. Klimes T, Sebokova E. Hypertension and the insulin resistance syndrome of rats. Are they related? Ann NY Acad Sci 1997; 87: 13-34.

52. Reaven GM. Syndrome X: 6 years later. J Intern Med 1994; 236 (Suppl. 736): 13-22.

53. DeFronzo R, Farranni E. Insulin resistance. A multi-faceted syndrome responsible of N1DDM, obesity, hypetension, dyslipidemia, and atherosclerotic cardiovascular disease. Diabetes Care 1991; 14: 175-94.

54. Reddy SSK. Reducing the incidence of coronary heart disease by managing hypertension: Implications of syndrome X. Can J Pub Health 1994; 85(Suppl. 2) S51-3.

55. Wajchenberg BL, Malerbi DA, Rocha MS, Lerario AC, Santomauro AT. Syndrome X: A syndrome of insulin resistance. Epidemiological and clinical evidence. Diabetes Metab Rev 1994; 10(l):19-29.

56. Fuh MM, Yin SS, Pei D et al: Resistance to insulin mediated glucose uptake and hyperinsulinemia in women who had preeclampsia during pregnancy. Am J Hypertens 1995;8 (7):768-71.

57. Laivuori H, Tikkanen MJ, Ylikorkala O. Hyperinsulinemia 17 years after preeclmaptic first pregnancy. J Clin Endocrinol Metab 1996; 81(8):2908-2911.

58. Rowe J, Young J.Minaker K, Stevens A, Palotta J.,Landsberg L. Effect of insulin and glucose infusions on sympathetic nervous system activity in normal man. Diabetes 1981; 98(30)219-25.

59. Axelrod L. Insulin, prostaglandins, and the pathogenesis of hypertension. Diabetes 1991; 40: 1223-7.

60. Roberts JM. Pregnancy - related hypertension. In: Creasy R, Resink R, eds. Maternal - Fetal Medicine. Principles and Practice. Second ed. Philadephia: W.B. Saunders, 1989: 777-824.

61. Friedman SA, Taylor RN, Roberts JM. Pathophysiology of preeclampsia. Clin Perinatol 1991; 18(4):661-82.

62. Lyall F, Greer IA. Pre-eclampsia: a multifaceted vascular disorder of pregnancy. J Hypertens 1994; 12: 1339-45.

63. McCarty MF. Hemostatic concomitants of Syndrome X. Med Hypotheses 1995; 44: 179-93

64. Pershadsingh H, Szollosi J, Benson S, Hyun W, Feuerstein B, Kurtz T.Effects of ciglitazone on blood pressure and intracellular calcium metabolism. Hypertension 1993 ;21(6,Pt2): 1020-3.

65. Zemel M, Zemel P,Berry S et al.Altered platelet calcium metabolism as an early predictor of increased peripheral vascular resistance and pre eclampsia in urban black women.N Eng J Med 1990:323:434-8

66. Zenel MJohnson B, Zemel P. Calcium transport and insulin resistance in pregnancy induced hypertension.Hypertension 1990 ; 16:318

67. Steiner G. Hyperinsulinaemia and hypertriglyceridaemia J Intern Med 1994; 236 (Suppl. 736): 23-6.

68. Davidson DM. Preventive Cardiology. Baltimore: Williams and Wilkins, 1991.

69. Despres J-P, Lemieux S, Lamarche B, Prud D, Moorjani S, Burn L-D et al. The insulin resistance - dyslipidemic syndrome: Contribution of visceral obesity and therapeutic implications. Int J Obes 1995; 19 (suppl 1): S76-S86.

70. Solomon CG, Caroll JS, Okumura K, Graves SW, Seely EW. Higher cholesterol and insulin levels are associated with increased risk for pregnancy induced hypertension Am J Hypertens. 1999;12:276-82

71. Defronzo RA, The effect of insulin on renal sodium metabolism. Diabetologia 1981;21:165-171.

72. Feldman RD, Bicrbrier GS. Insulin - mediated vasodilation : impairment with increased blood pressure and body mass. Lancet 1993; 342: 707-709

73. Kaaja R, Tikkanten MJ, Vinikka L, Ylikorkala O. Serum lipoproteins, insulin ,and urinary prostanoid metabolites in normal and hypertensive pregnant women. Obstet Gynecol 1995;85:353-356.

74. Kaplan NM. The Deadly Quartet. Arch Intern Med 1989; 149: 1514-1520.

75. Sowers JR. Saleh AA, Sokol RJ. Hyperinsulinemia and insulin resistance are associated with preeclampsia in African-Americans. Am J Hypertens 1995; 8: 1-4.

76. Martinez Abundis E, Gonzalez Ortiz M, Quinoncs Galvan A ,Ferrkkannini E. Hyperinsulincmia in glucose tolerant women with preeclampsia. A controlled study. Am J Hypertens. 1996;9:610-14.

77. Solomon CG, Sccly EW. Brief review : Hypertension in Pregnancy.A manifestation of insulin resistance syndrome? Hypertension 2001:37;232-39.

78. Cioffi FJ, Amorosa Lf, Vintzileos AM. et al. Relationship of insulin resistance and hyperinsulincmia to blood pressure during pregnancy. J Matern Fetal Med. 1997;6:174-179.

79. Wolf M, Sandler L, Munioz K, Hsu K, Ecker JL, Thadhani R. First trimester insulin resistance and subsequent preeclampsia: prospective study. J clin Endocrinol Mctab. 2002;87:1563-68.

80. Yu CJH, Papageor ghion AT, Bindra R, Spencer K, Nicolaides KH. Second trimester sex hormone binding globulin and subsequent development of preeclampsia. J Meternal -fetal and neonat Med. 2007; 16(3): 158-62.

81. Parrctti E, Lapolla A, Dalfra MG, Pacini G, Mari A, Coini R ct al. Preeclampsia in lean Normotensive normotolerant pregnant women can be predicted by simple insulin sensitivity indixes. Hypertension. 2006:47:449-53.

82. Lakso M. How good a marker is insulin level for insulin resistance? Am J. Epidemiol 1993; 137 (9):959-65

83. Kalpan NM. Clinical hypertension. 6^{1} ed. Lippincott Williams and Wilkins. 1994:90.

84. Modan M, Halkin H, Almog S et al. Hyperinsulincmia: a link between hypertension obesity and glucose intolerance. J Clin Invest 1985;75:809-17

85. Nichols AL, Nelson JC. Radioimmunoassay. Ma San Pedro Calif. Nichols Institute. JAMA. 1977.

86. Shohreh. M, Bijan K. Insulin changes in preeclamptic women during pregnancy. Ann Saudi Med 2004; 24(6): 434-36.

87. Lei Q, Lj Lv, et al, Ante- partum and post- partum markers of metabolic syndrome in pre-eclampsia. Journal of human hypertension (2011) 25, 11-17.

88. Hamashki T, Yashui 1 ,Hirai M, Masuzaki 11, Issuhimaru T. hyperinsulinemia increases the risk of gestational hypertension Int. I. Gynaecol Obster 1996, 55, 141:146.

89. Tripathy C.Malik S.Shah P, Lakshmi R, Tripathy D.Serum Insulin and lipid profile in Normal pregnant and pregnancy induced Hpertensive women from North IndiaiAnst NZ J Obstet Gynecol l999;39:3:321-23.

Annexures

PROFORMA

- NAME:
- AGE
- OCCUPATON
- IP NO.
- DOA:
- DOD
- GPL A
- LMP
- EDD
- Gestational age at the time of sampling :

History

Present pregnancy-time of detection of PIH

Obstetric History - Past H/o PIH

Past History : Any history of Chronic hypertension, Diabetes Mellitus, Renal disease, Cardiac disease.

Family History : Any family history of PIH

O/E

Height :

Weight :

BMI :

Pallor:

Edema :

Icterus:

BP:

Systemic Examination

Obstetric Examination

Investigation :

Routine antenatal investigations - HB

HIV

HBsAg

VDRL

Blood group

Urine routine and micro

Random blood sugar

Platelet Count

RFT

LFT

Serum Uric Acid

Fasting Plasma Insulin

ABBREVIATIONS

ADP	-	Adenosine Diphosphate
ALP	-	Alkatine Phosphatase
ALT	-	Alanine Amino Transferase
AST	-	Aspartate Amino Transferase
ATP	-	Adenosine Triphosphate
BMI	-	Basal Metabolic Index
BP	-	Blood Pressure
Ca^{++}	-	Calcium
DM	-	Diabetes Mellitus
EDRF	-	Endothelium Derived Relaxing Factor
FFA	-	Free Fatty Acids
GFR	-	Glomerular Filtration Rate
Glut-2	-	Glutamate -2 Carrier
GTT	-	Glucose Tolerance Test
HDL	-	High Density Lipoprotein
IGF-1	-	Insulin like Growth Factor - 1
IgG	-	Immunoglobulin G
Igl	-	Immunoglobulin I
IRS	-	Insulin Resistance Syndrome
LDH	-	Lactate Dehydrogenase
LDL	-	Low Density Lipoprotein

NHBPEP	-	National High Blood Pressure Education Programme
NIDDM	-	Non insulin Dependent Diabetes Mellitus
NO	-	Nitric Oxide
PAI-1	-	Plasminogen Activator Inhibitor -1
PAI-2	-	Plasminogen Activator Inhibitor - 2
PGE2	-	Prostaglandin E2
PGI_2	-	Prostaglandin I_2
PIH	-	Pregnancy induced Hypertension
rpm	-	Rotation per minute
SHBG	-	Sex Hormone Binding Globulin
TGS	-	Triglycerides
TXA2	-	Thromboxane A_2

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI 600 003

EC Reg.No.ECR/270/Inst./TN/2013
Telephone No.044 25305301
Fax: 011 25363970

CERTIFICATE OF APPROVAL

To

Dr.P.S.Kotteeswari
II Year PG in MS (O & G)
Institute of Obstetrics and Gynaecology
Egmore
Chennai 600 008

Dear Dr.P.S.Kotteeswari,

The Institutional Ethics Committee has considered your request and approved your study titled **"COMPARATIVE STUDY OF FASTING PLASMA INSULIN LEVEL BETWEEN NORMOTENSIVES AND PREECLAMPTIC WOMEN "** NO.09102014.

The following members of Ethics Committee were present in the meeting hold on 07.10.2014 conducted at Madras Medical College, Chennai 3.

1. Dr.C.Rajendran, MD	:Chairperson
2. Dr.R.Vimala,MD.,Dean,MMC,Ch-3	: Deputy Chairperson
3. Prof.B.Kalaiselvi,MD.,Vice Principal,MMC,Ch-3	: Member Secretary
4. Prof.R.Nandhini,MD.,Inst.of Pharmacology,MMC	: Member
5. Prof.K.Ramadevi, Director I/c,Inst.of Bio-Chem.MMC	: Member
6. Prof.Saraswathy,MD.,Director,Pathology, MMC	: Member
7. Prof.S.G.Sivachidambaram,MD.,Director I/c Inst.of Internal Medicine,MMC	: Member
8. Thiru S.Rameshkumar, Administrative Officer	: Lay Person
9. Thiru S.Govindasamy, BA., BL.,	: Lawyer
10.Tmt.Arnold Saulina, MA., MSW.,	: Social Scientist

We approve the proposal to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

21/10/14

Member Secretary – Ethics Committee

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE
CHENNAI-600 003

Sys 2

INFORMATION SHEET

Name of the Study : Date :

Name of the Investigator : IP No. :

Name of the Participant :

Name of the Institute :

- We are conducting a study to compare the fasting plasma insulin level between the normotensive and preeclamptic antenatal mothers.
- If found to have high fasting insulin level we may have to perform certain additional test which is no way would be affecting your management or treatment.
- The privacy of the patients in the research will be maintained throughout the study.
- In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.
- Taking part in the study is voluntary. You are free to decide whether to participate in the study or with draw at any time. Your decision will not result in any loss of benefits to which you are otherwise entitled.
- The results of the special study may be intimated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management or treatment.

Investigator Signature: Participant Signature:

CONSENT FORM

Name of the Study :

Date :

Name of the Investigator :

IP No. :

Name of the Participant :

Name of the Institute :

The details about this study have been explained to me. I am fully aware of this study and I am accepting to undergo all investigations needed for this study.

I am accepting to take blood samples needed for this study.

After fully understanding the procedures and I give full consent for the procedures without any undue pressure from anybody. I am aware that my participation in the study is voluntary and I can withdraw from this study at any time during this study period without giving any reason, without the medical care that will normally be provided by the hospital being affected.

I agree not to restrict the use of any data or results arises from this study provided such a uses only for the scientific purpose.

I have been given an information sheet giving details of the study.

I fully consent to participate in the above study.

I received the details about the study on Fasting plasma insulin level in relation with severity of preeclampsia.

Investigator Signature:

Participant Signature:

Relatives Signature:

ஆராய்ச்சி தகவல் தாள்

ஆராய்ச்சி தலைப்பு

"கர்ப்பிணி பெண்களுக்கான உயர்ரத்த அழுத்தத்தின் தீவிர விளைவுகளை முன்கூட்டியே அறிவதற்கான இரத்தப்பரிசோதனைப் பற்றிய ஒரு ஆராய்ச்சி"

ஆராய்ச்சியாளர் பெயர் : தேதி :

பங்கேற்பாளர் பெயர் : உள் நோயாளி எண் :

ஆராய்ச்சி நடைபெறும் இடம் :

அரசு பொது தாய்சேய் நல மருத்துவமனையில் நாங்கள் கர்ப்பிணி பெண்களுக்கான உயர்ரத்த அழுத்தத்தின் தீவிர விளைவுகளை முன்கூட்டியே அறிவதற்கான இரத்தப்பரிசோதனை முறைகளை ஒப்பிடுகிறோம்.

இந்தப் புதிய முறையானது, புதியதாக எந்தவிதமான பக்க விளைவையோ, தாய்சேய் இருவரின் உடல்நலத்திற்கு எந்தவித பாதிப்பையோ ஏற்படுத்தாது.

முடிவுகளை அல்லது கருத்துக்களை வெளியிடும் போதோ அல்லது ஆராய்ச்சியின் போதோ தங்களது பெயரையோ அல்லது அடையாளங்களையோ வெளியிடமாட்டோம் என்பதைத் தெரிவித்துக் கொள்கிறோம்.

இந்த ஆராய்ச்சியில் பங்கேற்பது தங்களுடைய விருப்பத்தின் பேரில்தான் இருக்கிறது. மேலும் நீங்கள் எந்நேரமும் இந்த ஆராய்ச்சியிலிருந்து பின்வாங்கலாம் என்று தெரிவித்துக்கொள்கிறோம்.

இரத்தப்பரிசோதனையின் முடிவு இந்த ஆராய்ச்சியின் முடிவின்போது தங்களுக்கு அறிவிக்கப்படும். இரத்தப்பரிசோதனையில் ஏதேனும் மாறுதல் இருந்தாலும் அது தங்களது சிகிச்சை முறையில் எந்தவித பாதிப்பையும் ஏற்படுத்தாது என்பதை தெரிவித்துக்கொள்கிறேன்.

ஆராய்ச்சியாளர் கையொப்பம் பங்கேற்பாளர் கையொப்பம்

ஆராய்ச்சி ஒப்புதல் கடிதம்

ஆராய்ச்சி தலைப்பு

“கர்ப்பிணி பெண்களுக்கான உயர்ரத்த அழுத்தத்தின் தீவிர விளைவுகளை முன்கூட்டியே அறிவதற்கான இரத்தப்பரிசோதனைப் பற்றிய ஒரு ஆராய்ச்சி”

ஆராய்ச்சியாளர் பெயர் : தேதி :

பங்கேற்பாளர் பெயர் : உள் நோயாளி எண் :

ஆராய்ச்சி நடைபெறும் இடம் :

இந்த ஆராய்ச்சியின் விவரங்களும் அதன் நோக்கங்களும் முழுமையாக எனக்கு தெளிவாக விளக்கப்பட்டது.

எனக்கு விளக்கப்பட்ட விஷ்ங்களை நான் புரிந்துக்கொண்டு எனது சம்மதத்தை தெரிவிக்கிறேன்.

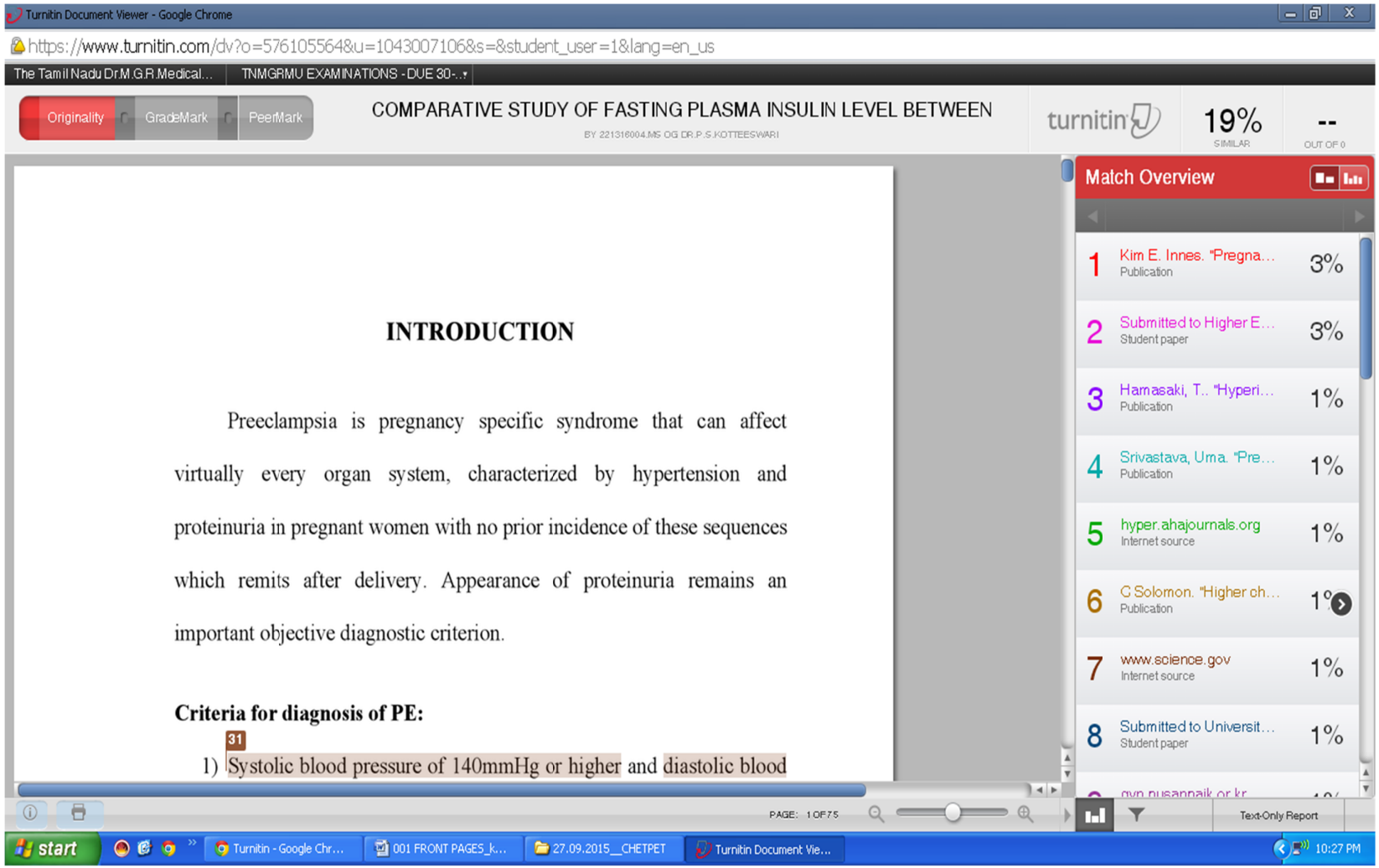
எனக்கு இரத்தப் பரிசோதனை செய்துகொள்ள சம்மதம்.

இந்த ஆராய்ச்சியில் பிறரின் நிர்பந்தமின்றி என் சொந்த விருப்பத்தின்பேரில் பங்கு பெறுகின்றேன். இந்த ஆராய்ச்சியில் இருந்து நான் எந்நேரமும் பின்வாங்கலாம் என்பதையும் அதனால் எந்த பாதிப்பும் ஏற்படாது என்பதையும் நான் புரிந்துகொண்டேன்.

உயர்ந்த அழுத்தத்தின் தீவிர விளைவுகளை முன்கூட்டியே அறிவதற்கான இரத்தப்பரிசோதனை குறித்த இந்த ஆராய்ச்சியின் விபரங்களைக் கொண்ட தகவல் தாளைப் பெற்றுக்கோண்டேன்.

நான் என்னுடைய சுய நினைவுடனும் மற்றும் முழு சுதந்திரத்துடனும் இந்த மருத்துவ ஆராய்ச்சியில் என்னை சேர்த்துக்கொள்ள சம்மதம் தெரிவிக்கிறேன்.

ஆராய்ச்சியாளர் கையொப்பம் பங்கேற்பாளர் கையொப்பம்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INTRODUCTION
Preeclampsia is pregnancy specific syndrome that can affect virtually every organ system, characterized by hypertension and proteinuria in pregnant women with no prior incidence of these sequences which remits after delivery. Appearance of proteinuria remains an important objective diagnostic criterion.
Criteria for diagnosis of PE:
1) Systolic blood pressure of 140mmHg or higher and diastolic blood
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INTRODUCTION

Preeclampsia is pregnancy specific syndrome that can affect virtually every organ system, characterized by hypertension and proteinuria in pregnant woman with no prior incidences of these conditions which curtails after delivery. Appearance of proteinuria remains an important objective diagnostic criterion.

Criteria for diagnosis of PE:

1) Systolic blood pressure of 140mmHg or higher and diastolic blood pressure of 90mmHg or higher that occurs after 20wks of gestation in a woman with previously normal BP.

2) Proteinuria defined as urinary excretion of 0.3g protein or higher in a 24hrs urine specimen.

PE associated with abnormal or dysfunctional placentation leading to increased vascular resistance and reduced placental perfusion. These changes are due to endothelial dysfunction. However the factor that cause the disturbance has not been identified.

1

MASTER CHART - CASES

Sl.No	Name	Age	DOA	Ip.No	POG	Parity	BMI	Mild PE	Severe	Fasting Insulin
1	Mahalakshmi	26	10/6/2014	25889	37	Multi	24.18		Yes	27.03
2	Selvi	24	10/6/2014	26302	35+2	Primi	25.33	Yes		3.8
3	Poongodi	23	11/5/2014	29659	38	Primi	23.04		Yes	47.4
4	Rajeswari	31	11/7/2014	29661	32+5	Primi	19.8		Yes	24.36
5	Rekha	27	11/14/2014	30617	30	Multi	22.12		Yes	30.05
6	Bommi	25	11/15/2014	29699	38	Primi	30.09		Yes	17.81
7	Kotteeswari	30	12/2/2014	32065	33+2	Primi	24.81	Yes		9.03
8	Gayathri	26	12/9/2014	33996	36	Primi	23.26		Yes	39.2
9	Parimala	28	12/22/2014	35516	30+5	Multi	27.12	Yes		8.16
10	Manjula	29	1/5/2015	36959	29+3	Primi	22.6		Yes	28.9
11	Vijaya	35	1/5/2015	36738	37+4	Primi	24.1		Yes	32.14
12	Shanthi	29	1/12/2015	525	30	Multi	25.3		Yes	28.25
13	Alamelu	22	1/19/2015	1266	36+5	Primi	28.2	Yes		8.78
14	Maheshwari	29	1/19/2015	1307	28+3	Primi	24.6		Yes	27.08
15	Nagajothi	28	2/2/2015	2501	37	Multi	23.4	Yes		3.03
16	Soniya	27	2/6/2015	2273	31+1	Primi	26.15		Yes	43.2
17	Rajaponni	20	2/9/2015	3150	33+2	Primi	27.6		Yes	25.04
18	Sheela	34	2/9/2015	3134	32+3	Primi	26.12		Yes	27.12
19	Vijayalakshmi	32	2/27/2015	4038	33+5	Primi	20.07		Yes	10.7
20	Devi	25	3/11/2015	6197	30+1	Primi	21.42		Yes	37.84
21	Kalaiselvi	32	3/12/2015	6323	30+5	Primi	19.18		Yes	27.12
22	Geethakumari	27	3/12/2015	6247	34+3	Primi	20.09	Yes		3.8
23	Archana	21	3/13/2015	6503	37+4	Multi	21.78	Yes		8.78
24	Lakshmi	32	3/16/2015	6770	36+2	Multi	26.9		Yes	29.08
25	Avanthika	22	3/19/2015	7046	37	Primi	22.6	Yes		9.2
26	Malarvzhi	20	4/1/2015	7775	32	Primi	27.18	Yes		7.64
27	Susaimary	28	4/1/2015	8275	37+1	Primi	26.14		Yes	28.9
28	Punitha	21	4/3/2015	8484	38	Multi	23.66	Yes		7.64
29	Ambika	27	4/5/2015	8579	33+2	Primi	28.77		Yes	30.05
30	Ganga	35	6-Apr	8661	36	Primi	29.2		Yes	11.81
31	Manimegalai	21	4/6/2015	8637	30+1	Primi	22.18		Yes	24.36
32	Durga	23	4/11/2015	9499	32+2	Primi	28.1		Yes	29.75
33	Lavanya	19	4/15/2015	9705	37+6	Multi	24.6	Yes		6.54
34	Rajalakshmi	28	4/15/2015	9806	37	Primi	28.3		Yes	27.7
35	Banumathi	21	4/16/2015	9873	33+1	Primi	22.69		Yes	18.16
36	Parimala	27	4/20/2015	10295	30+3	Multi	22.16		Yes	28.01

Sl.No	Name	Age	DOA	Ip.No	POG	Parity	BMI	Mild PE	Severe	Fasting Insulin
37	Rubhini	34	4/21/2015	10409	29+2	Primi	25.2	Yes		7.84
38	Sheeba	33	4/21/2015	10415	36	Primi	29.4	Yes		8.2
39	Surya	24	4/26/2015	10871	32+5	Multi	28.8		Yes	17.12
40	Fathimaparveen	26	4/29/2015	11249	33	Multi	21.7		Yes	26.44
41	Ramya	30	5/1/2015	11390	37+1	Primi	23.12		Yes	23.72
42	Boomadevi	25	5/1/2015	11412	32	Primi	24.18		Yes	29.48
43	Radha	24	5/6/2015	11625	29+6	Primi	23.29	Yes		7.12
44	Sharmili	20	5/7/2015	12199	26+1	Primi	22.87	Yes		8.13
45	Chandra	22	5/10/2015	12549	30+2	Multi	22.14	Yes		9.19
46	Ammu	40	5/10/2015	12574	35	Primi	23.76		Yes	34.26
47	Krishnaveni	22	5/12/2015	12639	31+2	Primi	22.19	Yes		14.16
48	Chithradevi	28	5/14/2015	12988	27	Multi	22.18	Yes		7.33
49	Sathya	25	5/15/2015	13237	32	Multi	26.15	Yes		4.16
50	Pappy	19	5/18/2015	13569	34+5	Primi	24.86		Yes	25.22
51	Sangeetha	20	5/22/2015	14169	35+6	Primi	26.79		Yes	11.87
52	Renugadevi	29	5/27/2015	14829	30+1	Multi	24.57		Yes	29.37
53	Janagi	35	5/30/2015	15135	32	Primi	22.81		Yes	32.19
54	Gandhimathi	28	6/1/2015	15336	30+2	Primi	28.18		Yes	6.3
55	Rukmani	30	6/1/2015	15201	37+6	Multi	28.72	Yes		6.12
56	Ramya	24	6/2/2015	15380	35	Primi	27.55		Yes	14.06
57	Poongodi	27	6/2/2015	15417	36+2	Primi	26.12	Yes		6.3
58	Chandrika	34	6/2/2015	15399	33+3	Primi	26.76		Yes	27.12
59	Sarasvathi	29	6/3/2015	16001	29	Primi	24.56	Yes		8.34
60	Devaki	23	6/5/2015	16341	36+2	Primi	20.12		Yes	24.12
61	Manjula	29	6/7/2015	16569	34	Multi	26.13		Yes	28.4
62	Dhanalakshmi	32	6/9/2015	17309	37+3	Primi	25.01		Yes	25.23
63	Meenakchi	27	6/15/2015	18443	30+6	Primi	27.81		Yes	23.71
64	Shanthi	34	6/20/2015	19804	29+4	Primi	26.12		Yes	29.4
65	Punitha	22	7/1/2015	19888	36	Multi	23.88	Yes		7.12
66	Thilagavathi	24	7/5/2015	23164	35+4	Primi	26.7		Yes	25.48
67	Vijayalakshmi	29	7/6/2015	24239	37	Primi	25.12		Yes	11.87
68	Manimegalai	36	7/10/2015	25166	37+5	Primi	29.15		Yes	48.1
69	Rajamma	31	7/10/2015	25004	31	Multi	22.48		Yes	24.27
70	Ashtalakshmi	27	7/15/2015	26856	29+6	Primi	27.18	Yes		6.16

MASTER CHART - CONTROL

Sl.No	Name	Age	DOA	Ip.No	POG	Parity	BMI	Normotensive	Mild PE	Severe PE	Fasting insulin Level
1	Vetriselvi	24	10/6/2014	25718	37	Primi	20.6	Yes	-	-	0.1
2	Kasthuri	33	11/15/2014	29661	36+4	Primi	21.92	Yes	-	-	1.1
3	Hemalatha	21	11/30/2014	31513	35	Primi	23.26	Yes	-	-	0.8
4	Muthulakshmi	24	12/24/2014	33128	37+2	Primi	26.48	Yes	-	-	1.8
5	Thavamani	20	1/1/2015	35396	38	Primi	21.24	Yes	-	-	2.1
6	Geetha	18	1/30/2015	1820	30	Primi	20.06	Yes	-	-	0.9
7	Indhra	27	2/14/2015	3487	35+1	Multi	21.29	Yes	-	-	2.7
8	Gowri	27	2/15/2015	3767	37	Multi	26.34	Yes	-	-	6
9	Radha	30	2/28/2015	4109	36+6	Multi	20.17	Yes	-	-	1.6
10	Anjalai	20	3/2/2015	4136	37+4	Primi	23.26	Yes	-	-	0.3
11	Priyanka	32	3/6/2015	5001	38	Multi	24.12	Yes	-	-	2.5
12	Geethanjali	19	3/15/2015	6593	37+3	Primi	25.36	Yes	-	-	1.17
13	Victoriya	22	4/6/2015	8775	34	Primi	27.01	Yes	-	-	6.3
14	Arputhavalli	29	4/7/2015	8914	36	Multi	30.23	Yes	-	-	0.7
15	Radha	24	4/10/2015	9429	35	Primi	24.33	Yes	-	-	5.3
16	Sudha	28	4/19/2015	10200	30	Multi	27.03	Yes	-	-	2.4
17	Kamatchi	31	4/30/2015	11349	31+2	Primi	27.33	Yes	-	-	4.3
18	Nirmaladevi	33	5/2/2015	11436	33	Multi	26.22	Yes	-	-	1.33
19	Malinidevi	32	5/6/2015	12001	37	Primi	19.8	Yes	-	-	1.18
20	Asha	28	5/20/2015	13798	36+4	Multi	24.03	Yes	-	-	2.27
21	Baby	33	5/26/2015	14243	32+4	Multi	29.27	Yes	-	-	3.96
22	Sivayogasundhari	24	6/1/2015	15232	31	Primi	23.18	Yes	-	-	4.32
23	Savitha	26	6/5/2015	16146	33+2	Multi	24.58	Yes	-	-	6.14
24	Krishnapriya	29	6/10/2015	17459	35	Multi	26.22	Yes	-	-	0.9
25	Veerammal	22	6/15/2015	18323	37	Primi	28.16	Yes	-	-	0.4
26	Aishabegam	21	6/21/2015	19849	38	Multi	23.24	Yes	-	-	1.17
27	Sarala	19	7/1/2015	20137	34+1	Primi	28.1	Yes	-	-	0.53
28	Sindhuja	34	7/3/2015	22841	35+6	Multi	26.13	Yes	-	-	0.98
29	Chithra	31	7/3/2015	22609	36+2	Multi	28.2	Yes	-	-	1.1
30	Sarasvathi	24	7/15/2015	26812	37	Multi	23.1	Yes	-	-	2.9

KEY TO MASTER CHART

DOA	-	Date of Admission
IP NO.	-	Inpatient Number
POG	-	Period of gestation
BMI	-	Basal Metabolic Index
Mild PE	-	Mild pre eclampsia
Severe PE	-	Severe pre eclampsia